VOLUME 51 NUMBER 1 JANUARY, 1961

AMERICAN JOURNAL
OF
OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

CONTENTS

Ophthalmic anesthesia ..... *Walter S. Atkinson* 1
Mistaken diagnoses in meningioma ..... *C. W. Rucker and T. P. Kearns* 15
Peripheral uveitis ..... *R. J. Brockhurst, C. L. Schepens and I. D. Okamura* 19
Modified Smith technique ..... *Richard A. Ellis* 26
Familial retinal detachment ..... *A. I. Friedman and E. Epstein* 33
Methods for lid separation ..... *Paul U. Fechner* 35
Inactivation of herpes-simplex virus ..... *T. W. Sery and F. P. Furgiuele* 42
Heparin in macular degeneration ..... *N. F. Schwilk, Jr., and A. J. Rosenberg* 57
Erythema nodosum ..... *James L. McCarthy* 60
Scleromalacia perforans ..... *J. Reimer Wolter and Maxwell D. Bentley* 71
Eye protection against small missiles ..... *George M. Stewart* 80
Localization of Diamox-S^{35} ..... *S. B. Goren, F. W. Newell and J. J. O'Toole* 87
Philippine ophthalmology ..... *Geminiano de Ocampo* 93
Chymotrypsin in surgery ..... *W. L. Hughes, E. L. Lewis and Joseph Amdur* 103
Chymotrypsin in strabismus surgery ..... *Edward G. Fortier* 106
Basic phenomena of retinopexy ..... *Henry A. Knoll* 113
Sutures in surgery of cornea ..... *Samuel D. McPherson, Jr.* 118
Von Hippel-Lindau disease ..... *Maxwell Thomas and Ronald M. Burnside* 140
Alpha chymotrypsin and foreign bodies ..... *Henry L. Hilgartner and Hardy E. Thompson, Jr.* 147
Posterior embryotoxon ..... *Frederick C. Wuest and Wayne L. Erdbrink* 148
Scleral rigidity determinations ..... *J. William Rogers and Winston Roberts* 150
Bilateral nuclear ophthalmoplegia ..... *R. Douglas Collins* 152
Papilloma of limbus ..... *B. M. Chatterjee* 154
Sympathetic ophthalmia ..... *Adalbert Fuchs* 156
Eye-dressing tray ..... *Y. A. Staton* 158
Departments 159

For a complete table of contents see page xxxv

Publication office: Curtis Reed Plaza, Menasha, Wisconsin

Copyright, 1961, Ophthalmic Publishing Company, 664 North Michigan Avenue, Chicago 11, Illinois

Subscription price in United States twelve dollars yearly. In Canada and foreign countries fourteen dollars. Published monthly by the Ophthalmic Publishing Company. Subscription and Advertising Office: 664 North Michigan Avenue, Chicago 11, Illinois. Second class postage has been paid at the post office at Menasha, Wisconsin. Printed in U.S.A.

World's Largest Selection of Artificial Eyes

Complete Artificial Eye Service

- Eyes custom made—glass or plastic
- Eyes from stock sent on memorandum same day order received—glass or plastic
- Damaged or broken artificial eyes accurately matched
- Fitted to all types of motility implants
- Implants, X-Ray therapy shields, foreign body locators
- Superior Quality—Finest Workmanship

Serving the Profession Since 1851

Mager and Gougelman inc.

30 North Michigan Avenue, Chicago 2, Illinois : 120 E. 56th St., New York 22, New York

BOSTON • BUFFALO (Paul Gougelman Co.) • CLEVELAND • DETROIT • HOUSTON (Soper Bros.)
KANSAS CITY • MINNEAPOLIS • PHILADELPHIA • PITTSBURGH • ST. LOUIS • WASHINGTON

acute conjunctivitis before treatment

clinical photographs

truly soluble—for fast relief of inflammation

0.1% OPHTHALMIC SOLUTION

NeoDecadron®

DEXAMETHASONE 21-PHOSPHATE—NEOMYCIN SULFATE

INDICATIONS: Trauma—mechanical, chemical or thermal; inflammation of the conjunctiva, cornea, or uveal tract involving the anterior segment; allergy; blepharitis.

CAUTION: Steroid therapy should never be employed in the presence of tuberculosis or herpes simplex.

NeoDECADRON is also available as the ophthalmic ointment (.05%). Ointment and solution are available with dexamethasone 21-phosphate alone: DECADRON® Phosphate Ophthalmic Solution and DECADRON Phosphate Ophthalmic Ointment.

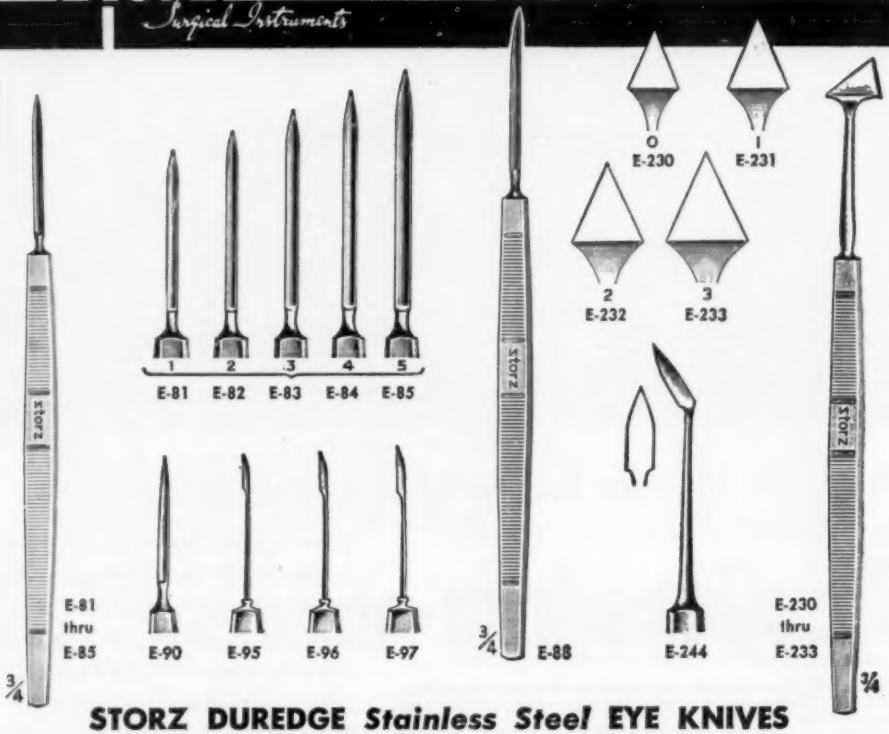
• unexcelled steroid activity • in true solution for peak effectiveness . . . maximal contact at the site of the lesion • superior patient comfort—no irritating particles • quick-acting, broad antimicrobial activity.

Additional information is available to physicians on request.
NeoDECADRON and DECADRON are trademarks of Merck & Co., Inc.

MERCK SHARP & DOHME
Division of Merck & Co., Inc., West Point, Pa.

4 days after treatment

storz
Surgical Instruments



STORZ DUREDGE *Stainless Steel* EYE KNIVES

Made of Special Alloy Cutlery Stainless Steel

Grain structure of this alloy is dense; holds a keen penetrating edge. Improved methods in hardening, tempering and honing plus this new Stainless Alloy Steel. Results: a superior knife.

E- 81*	Cataract Knife, VON GRAEFE: 25mm x 1.5mm.	$11.50
E- 82*	Cataract Knife, VON GRAEFE: 27mm x 1.7mm.	11.50
E- 83*	Cataract Knife, VON GRAEFE: 30mm x 2mm.	11.50
E- 84*	Cataract Knife, VON GRAEFE: 33mm x 2.3mm.	11.50
E- 85*	Cataract Knife, VON GRAEFE: 35mm x 2.5mm.	11.50
E- 88*	Cataract Knife, STORZ: a straight back medium size cataract knife with wafer thin blade for extreme sharpness and easy penetration.	15.00
E- 90*	Knife, Discision, WHEELER: 1mm x 18mm blade.	12.50
E- 95*	Knife Needle, ZIEGLER: 5mm.	11.50
E- 96*	Knife Needle, ZIEGLER: 6mm.	11.50
E- 97*	Knife Needle, ZIEGLER: 7mm.	11.50

STORZ DUREDGE *Stainless Steel* KERATOMES

E-230*	Keratome, JAEGER: size 0, angled, 8mm x 9½ mm.	$12.50
E-231*	Keratome, JAEGER: size 1, angled, 9½mm x 11mm.	12.50
E-232*	Keratome, JAEGER: size 2, angled, 11mm x 12½mm.	12.50
E-233*	Keratome, JAEGER: size 3, angled, 12½mm. x 14mm.	12.50
E-244*	Keratome, CASTROVIEJO: blade 13mm x 4mm, parallel portion of blade is not sharp.	13.50

Storz Duredge Stainless Steel and Duredge Carbon Steel cataract knives and keratomes are not imported; they are made only in our factory in St. Louis. All of our re-sharpening is also done in our factory by skilled instrument makers. *We do not utilize outside facilities for re-sharpening any eye knives.*

*Designates STAINLESS STEEL.

STORZ INSTRUMENT COMPANY • • • 4570 Audubon Ave., St. Louis, Mo.

New York Showroom—157 E. 64th St. at Lexington Ave.

eye examination in the morning back to work after lunch

MYDRIACYL™ 0.5% TROPICAMIDE 1.0%

With Mydriacyl, patients recover accommodation faster, return to work sooner. Fair accommodation occurs within 3-4 hours, **complete** recovery within 3 hours . . . **without the aid of miotics.** And with a miotic such as Isopto® Carpine, recovery is much quicker. For **your** benefit, maximum mydriasis and cycloplegia occur within 20-25 minutes, and persist about 20 minutes.

Caution: Like any mydriatic, Mydriacyl should be used with caution in cases where the intraocular pressure is unknown or has been found to be high.

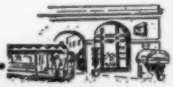
MYDRIACYL 0.5% for Mydriasis
(with moderate short-acting cycloplegia)

MYDRIACYL 1.0% for Cycloplegia

Supplied in both 7.5 cc. and 15 cc. Drop-Tainer® Dispensers.

Alcon **ALCON LABORATORIES, INC.** / FORT WORTH, TEXAS

PARSONS



World Headquarters for GONIOSCOPY and GONIOTOMY Instrumentation

Koeppe Diagnostic lens #6165

Goniotomy lens #6180

Operating Lamp on Stand #6140

6100	Floor gonioscope* with Haag-Streit microscope 15×	$390.00
6101	Stand only*	195.00
6102	Haag-Streit microscope 15× with nylon cord ceiling suspension	225.00
6151	Carrying case* for hand microscope and focal illuminator	19.50
6150	Barkan Focal Illuminator with plug-in transformer*	42.50
6165	Barkan Koeppe diagnostic lens, three sizes: 16-18-20 mm. lip diameters*	45.00
6175	Barkan Goniotomy lens (surgical) Infant size*	45.00
6180	Barkan Goniotomy lens (surgical) child-adult size*	45.00
6130	Barkan operating lamp,* hand model with transformer	72.50
6140	Barkan operating lamp,* floor model, built-in transformer	97.50
6191	Barkan Goniotomy knife (selected model)*	9.75

** Manufactured exclusively by Parsons Optical Laboratories.*

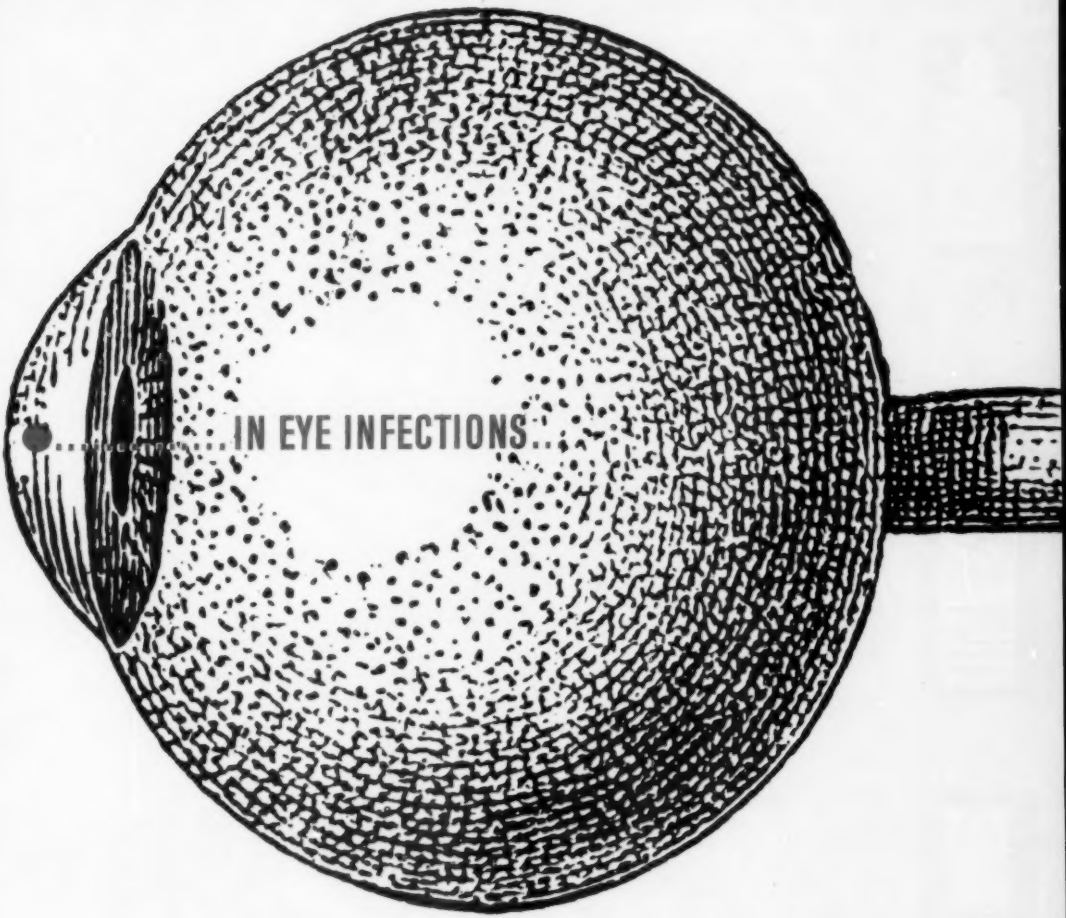
Floor Gonioscope #6160

Haag-Streit Hand Microscope for Gonioscopy #6127

Carrying Case for Hand Microscope and Focal Illuminator, #6151

PARSONS OPTICAL LABORATORIES

518 POWELL STREET · SAN FRANCISCO 2 CALIFORNIA



QUICK AND EFFECTIVE CONTROL WITH

OPHTHOCORT®

CHLOROMYCETIN® (chloramphenicol, Parke-Davis) – polymyxin B – hydrocortisone ophthalmic ointment

In the treatment of ocular infections, OPHTHOCORT Ophthalmic Ointment offers these significant therapeutic benefits: Prompt antibacterial and anti-inflammatory action • Good results against gram-negative as well as gram-positive invaders • Steroid protection against inflammation, discomfort, and possible scarring of ocular tissues • Virtual absence of irritative or allergic properties

OPHTHOCORT is intended for the topical treatment of ocular inflammation complicated by infection. It is administered by local application two to four times daily, as required.

OPHTHOCORT Ophthalmic Ointment contains 1% CHLOROMYCETIN (chloramphenicol, Parke-Davis), 0.5% hydrocortisone acetate, and 5,000 units polymyxin B sulfate per Gm.; supplied in ⅛-oz. tubes.

PARKE, DAVIS & COMPANY
DETROIT 32, MICHIGAN

25660

PARKE-DAVIS

Barnes-Hind WETTING SOLUTION

Sterile, non-irritating... optimal re-sterilizing[1] activity.

Formulated for freedom from ocular burning and stinging, Barnes-Hind Wetting Solution cleans and wets in one action. It is sterile, non-irritating. Its prolonged wetting-out action lubricates lenses efficiently all day, promotes desired floating effect, makes longer wearing possible. Active ingredient, benzalkonium chloride 0.004%.

SOQUETTE® SOLUTION

For sterile, antiseptic lens storage.

Storage in Soquette Solution prevents natural oils and ocular sebaceous secretions from drying onto the lens surfaces, and prepares the lenses for optimal wetting action. Blurring and irritation caused by drying-out of lenses are eliminated. Effectively antiseptic[1] for greater safety. Active ingredients, chlorobutanol 0.3% and benzalkonium chloride 0.004%.

DEGEST®

Soothes, refreshes, and clears ocular tissues.

Sterile Degest promptly relieves inflammation of ocular epithelial tissues which may result from excessive lens wearing. Ordinarily this condition subsides slowly. Degest brings about quick subjective relief. It contains phenylephrine hydrochloride 0.2% in a mildly hypertonic vehicle, benzalkonium chloride 0.01% and sodium bisulfite 0.1% as preservatives.

Cotton-Tipped MINIMS®

(Sterile Fluorescein Sodium 2%)

Convenient, safe, sterile... no wastage

Each Minims unit is a sterile disposable applicator designed for single-patient use. Supplied in containers of 20 individually over-wrapped Minims units.
TECHNIQUE OF APPLICATION:
Remove the over-wrap and squeeze the contents of the unit into the sterile cotton tip. Apply to the lower lid or bulbar conjunctiva. Discard the unit.

EFFECTIVE AIDS

to successful contact lens fitting/wearing

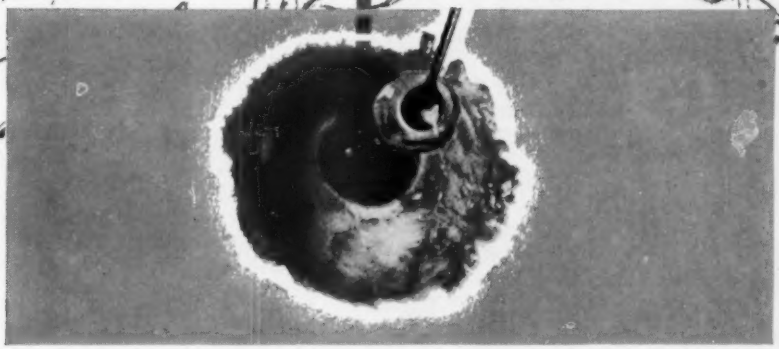
[1] CLIFTON, C. E. AND HALL, N. C. "RE-STERILIZING ACTIVITY OF CERTAIN CONTACT LENS SOLUTIONS." CONTACTO, THE CONTACT LENS JOURNAL, 3:10, 301-2, 1959.

Manufactured by **BARNES-HIND** OPHTHALMIC PRODUCTS, INC., 895 KIFER ROAD, SUNNYVALE, CALIFORNIA. REGENT 6-5462

ALPHA CHYMAR®

alpha chymotrypsin

TAKES "THE MOMENT OF ANXIETY" OUT OF CATARACT SURGERY[1]



ALPHA CHYMAR—lyophilized crystallized chymotrypsin—loosens the zonule fibers of the lens within minutes, and thus "can serve to relieve that moment of anxiety for the cataract surgeon when he meets up with a tough zonula. [ALPHA CHYMAR] helped to prevent the complications of capsule rupture and of undue zonular traction on structures of the inner eye."[1]

Data obtained in a double-blind study indicate "in an objective manner that alpha chymotrypsin definitely facilitates cataract extraction"[2] thus further confirming its value as a new adjunct in cataract surgery.[3,4,5,6]

Specifically packaged for zonule lysis in lens extraction, ALPHA CHYMAR is available in cartons of 5 packages. Each package contains a 5 cc. vial of lyophilized ALPHA CHYMAR and a 10 cc. vial of ALPHA CHYMAR DILUENT (Sodium Chloride Injection, USP).

1. Thorpe, H. E.: Am. J. Ophth. *49*:531-547 (Mar.) 1960. 2. Schwartz, B., *et al.*: Tr. Am. Acad. Ophth. & Otol. *64*:46-54 (Jan.-Feb.) 1960. 3. Cogan, J. E. H.: Proc. Roy. Soc. Med. *51*:927, 1958. 4. Jenkins, B. H.: J.M.A. Georgia *45*:431, 1956. 5. Raiford, M. B.: J.M.A. Georgia *48*:163, 1959. 6. Rizzuti, A. B.: Arch. Ophth. *61*:135, 1959.

ARMOUR PHARMACEUTICAL COMPANY
KANKAKEE, ILLINOIS

Armour Means Protection

© 1960 A.P. Co.

- **BROAD-SPECTRUM BACTERICIDAL ACTION**
- **ANTI-INFLAMMATORY ACTION**
- **RARELY SENSITIZES**

Topical hydrocortisone provides symptomatic relief of edema, pain and photophobia, and curbs neovascularization, while polymyxin B and neomycin eradicate most pathogens invading the eye, including Pseudomonas.

'CORTISPORIN'® brand OPHTHALMIC SUSPENSION

Each cc. contains:

'Aerosporin'® brand Polymyxin B Sulfate	10,000 Units
Neomycin Sulfate	5 mg.
Hydrocortisone (1%)	10 mg.

Indicated in bacterial, allergic, vernal and phlyctenular conjunctivitis; blepharitis; episcleritis; iritis; anterior uveitis; interstitial, sclerosing, postoperative or acne rosacea keratitis; chemical and thermal burns of the cornea.

Application: Apply 1 or 2 drops in the affected eye every 3 or 4 hours, depending upon the severity of the condition. In acute conditions, the drops may be used at more frequent intervals, if required.

Caution: Not recommended for herpes corneae (dendritic corneal ulcers) or conditions involving the posterior segment of the eye.

Available in bottles of 5 cc. with sterile dropper.

BURROUGHS WELLCOME & CO. (U. S. A.) INC., Tuckahoe, New York

Just as a reminder...

TO CONTROL ALL THE GLAUCOMAS SAFELY

EPITRATE®
L-EPHINEPHRINE BITARTRATE 2%

- stabilized
- fully active
- single strength

ALMOCARPINE®
PILOCARPINE HCl
½-1-2-3-4%

- no methylcellulose
- no wetting agents
- no additives

In Ocular Surgery ...

THE PERFECTED
steridroppa®

disposable single dose

guarantees
sterility and stability
AT THE MOMENT OF USE

Avoid Pyocyaneus Infection

USE
FLUOR I STRIP®

sterile fluorescein applicators

For delineating corneal injuries.
For determining site of intraocular injury.
For applanation tonometry.

OPHTHALMOS, Inc.
DIVISION OF DOHO
100 VARICK ST., NEW YORK 13 N. Y.
IN CANADA: DOHOW CHEMICAL CO., LTD., MONTREAL 3

Pharmacologic Research for the Care and Preservation of Vision

If you're thinking about doing contact lens work, or if you're having fitting problems . . .

INVESTIGATE THIS REMARKABLE AO CONTACT LENS INSTRUMENT PACKAGE

1. AO Ophthalmometer *measures radius of curvature of cornea.* Accurate measurements assured. Direct radius of curvature scale is engraved on wheel . . . no chance for error . . . bothersome conversion tables eliminated.

2. AO Radiuscope specifically designed to *measure radius of curvature of contact lens.* You can make extremely accurate readings easily and quickly . . . measure both lenses in less than 60 seconds. Radiuscope also permits surface inspection for microscopic irregularities and flaws.

3. AO Ultraviolet Hand Magnifier *for accurate contact lens fitting.* Conveniently portable...use from any angle. Magnifies the eye and brings out fluorescein pattern.

Combine the inherent accuracy of these three AO instruments with your own professional skills to insure accurate, comfortable fittings and patient satisfaction. Ask your AO Sales Representative, or Supplier about this complete contact lens instrument package, or write:

American Optical COMPANY

INSTRUMENT DIVISION, BUFFALO 15, NEW YORK

Dept. O 253

☐ Please send complete information on the AO Contact Lens Package.

☐ I would like a demonstration of AO instruments for Contact Lens Work.

Name_____

Address_____

City_____ Zone____ State_____

IN CANADA write—American Optical Company Canada Ltd., Box 40, Terminal A, Toronto, Ontario

A STANDARD IN THE MANAGEMENT OF GLAUCOMA

DIAMOX is indicated as an immediate emergency measure with miotics to lower intraocular pressure.[2,6] ■ DIAMOX promptly relieves pain[2] and improves medical or surgical prognosis by clearing corneal edema.[1] ■ DIAMOX minimizes the danger of surgical complications and increases the chance of success by reducing congestion preoperatively and maintaining low postoperative tension.[1,3] ■ DIAMOX provided more than 40 per cent decrease in aqueous flow in 83 per cent of 440 eyes with various glaucomatous conditions.[1] Other reports[4,5] also indicate a reduction of one-third to one-half. ■ DIAMOX was preferred on the basis of efficacy, toleration, or dosage levels in a comparison of four carbonic anhydrase inhibitors.[7]

Recommended Average Dosage in Glaucoma: One tablet, 250 mg., every four hours. Supplied: Scored tablets of 250 mg., bottles of 25 and 100. Vials of 500 mg. for parenteral use. ■ References: 1. Becker, B.: In: *Symposium on Glaucoma,* C. V. Mosby Company, St. Louis, 1959, p. 172. • 2. Benedict, W. H.: *M Times* 48:33 (Jan.) 1960 • 3. Carbajal, U. M.: *Eye, Ear, Nose & Throat Monthly* 39:60 (Jan.) 1960. • 4. Chandler, P. A.: *A.M.A. Arch. Ophth.* 62:1101 (Dec.) 1959. • 5. Duke-Elder, S.: *Canad. M. A. J.* 82:293 (Feb.) 1960. • 6. Gorrilla, V. L.: *Arizona Med.* 16:187 (Mar.) 1959. • 7. Henry, M. M., and Lee, P.: *Am. J. Ophth.* 47:199 (Feb.) 1959.

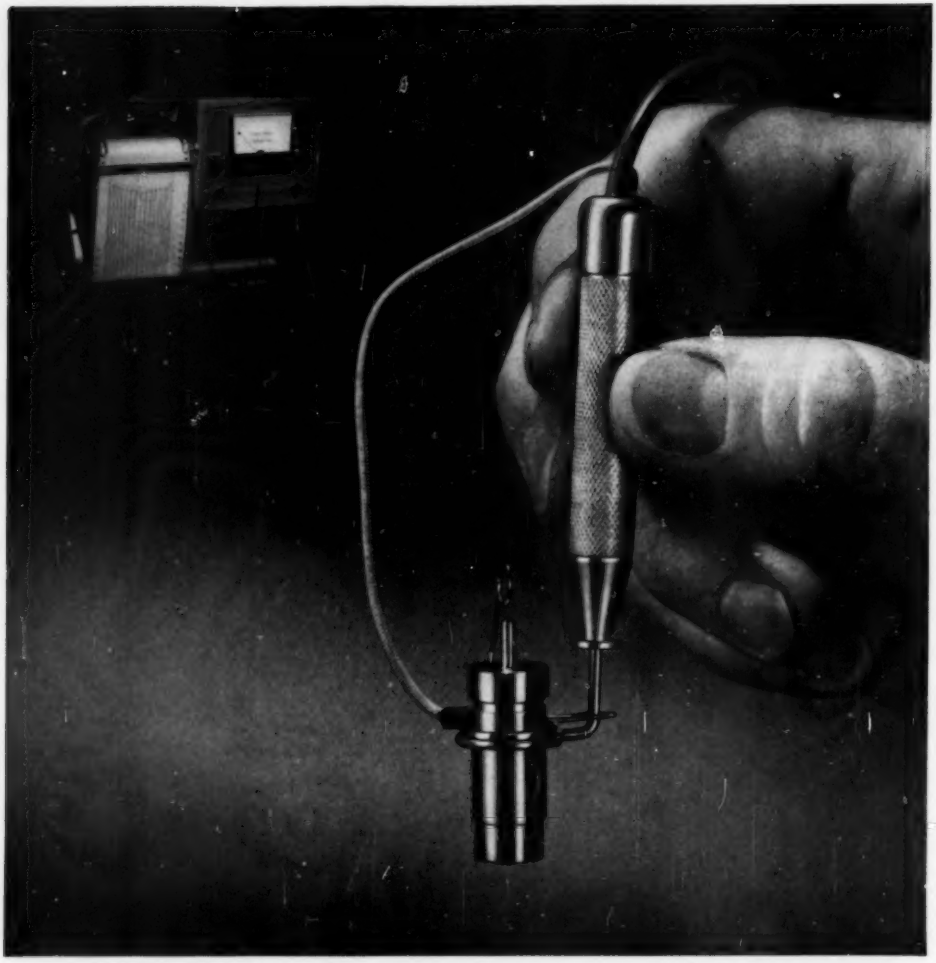
to lower intraocular pressure

DIAMOX®

Acetazolamide Lederle

in the acute glaucoma crisis

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York



to make the most of your talents and techniques...

TR Electronic Tonographer

The new *dual model*—improved Electronic Tonometer and synchronized direct-writing recorder in one compact unit—brings greater accuracy and ease to both routine tonometry and clinical tonography. Developed through V. Mueller research. New brochure upon request.

VMUELLER & CO.

Fine Surgical Instruments and Hospital Equipment Since 1895

330 S. HONORE STREET, CHICAGO 12, ILLINOIS

DALLAS • HOUSTON • LOS ANGELES • ROCHESTER, MINN.

Not:

a medical milestone

Not:

a revolutionary new drug

But:

an effective, adjunctive oral treatment of glaucoma

ALCON'S BRAND OF DICHLORPHENAMIDE

Oratrol

Oratrol joins Alcon Laboratories' family of fine products for glaucoma therapy. As a carbonic anhydrase inhibitor, Oratrol offers the advantage of oral treatment for glaucoma. It can be given alone or in combination with these preferred Alcon topical miotics—Isopto Carpine or Isopto Carbachol. Both provide prolonged miosis. Each Oratrol tablet contains 50 mg. dichlorphenamide. Supplied in bottles of 100 tablets.* **Oral control**

**Isopto Carpine is now available in a new 6% strength.*

Alcon *ALCON LABORATORIES, INC., Fort Worth, Texas*

the red eye

in "everyday" practice presents a series of so-called "minor" eye complaints often requiring immediate care to avoid more serious consequences. ISO-SOL® sterile ophthalmics provide complete therapy in the unique Lacrivial® and Dropperette® packaging. Several preparations most frequently indicated for common eye disorders are listed below.

UNIQUE STERILE LACRIVIAL®

1 – Self-disinfecting tip. Bacteriostatic medication retained to bathe and disinfect tip.

2 – Airtight seal. Preserves stability, sterility, avoids leaking and crystallization.

3 – Controllable drop orifice.

4 – Color-coded cap. Minimizes possibility of dispensing error.

TEARISOL® (15 cc. Lacrivial)
Sterile, artificial tears – soothe and lubricate to relieve burning and itching in dry eyes and nonspecific irritation; excellent as a contact lens fluid. A 0.45% solution of methylcellulose of uniform purity, with benzalkonium chloride; pH 6.4. (If hyperemia is present, TEAR-EFRIN® – Tearisol with phenylephrine HCl – will provide immediate, symptomatic relief.)

SULFACIDIN®(10 cc. Lacrivial) (1 cc. Dropperette)
An antibiotic chemotherapeutic agent indicated for external ocular infections, including conjunctivitis and prophylaxis following foreign body removal. Neomycin sulfate 0.5% and sodium sulfacetamide 10% in methylcellulose vehicle; expiration dated; pH 7.2.

M-Z® SOLUTION (15 cc. Lacrivial)
An astringent, decongestant, antiseptic and mild topical anesthetic; provides comfortable zinc medication; for mechanical and allergic conjunctivitis and nonspecific irritation. Zinc sulfate 0.22%; piperocaine HCl 0.75%; phenylephrine HCl 0.1%; methylcellulose and buffer q.s.; pH 6.5. (If surface analgesia is not required, PHENYLZIN® – zinc sulfate with phenylephrine HCl – is recommended.)

DACRIOSE® (120 cc. plastic irrigator)
Sterile, isotonic, low surface tension, irrigating solution for office and home use and for contact lens wearers. A stable saline with boric acid sodium carbonate buffer system; pH 6.5.

Complete ISO-SOL product list available on request.

ISO-SOL

THERE IS NO EQUAL IN QUALITY TO ISO-SOL BRAND STERILE SOLUTIONS

CROOKES-BARNES Laboratories, Inc., Wayne, New Jersey

two highly effective topical miotics

in glaucoma... potent, prolonged control of intraocular pressure

HUMORSOL*

DEMECARIUM BROMIDE

- more potent and longer acting than other miotics
- b.i.d. dosage schedule usually provides round-the-clock control
- because it is unusually potent, it may be uniquely useful in breaking up peripheral synechiae
- aqueous — isotonic with conjunctival fluid
- stable — refrigeration not required
- 0.25% solution in 5-cc. vial with dropper

in glaucoma and strabismus... simplified local therapy

FLOROPRYL®

ISOFLUROPHATE

- long-acting — in glaucoma, one instillation daily is often sufficient; in strabismus, one instillation every two days to one week
- highly potent — may be effective when other agents fail
- two topical dosage forms — 0.1% solution in peanut oil, in 5-cc. vials; 0.025% ointment, in 3.5 Gm. tubes

also available **DARANIDE**® DICHLORPHENAMIDE *for oral control of intraocular pressure, 50 mg. tablets*

For additional information, write Professional Services, Merck Sharp & Dohme, West Point, Pa.

MSD MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

NEW
BufOpto®

NEW, EXCLUSIVE

BELLOWS

PAK

Easy to use
Compact
Control flow

NEO-FLO

STERILE

OPHTHALMIC IRRIGATING SOLUTION

Neo-Flo is a non-irritating irrigating solution for use in Ophthalmology. For office irrigating procedures after tonometry, gonioscopy, removal of foreign bodies, use of Fluorescein. Neo-Flo is well suited for first aid treatment.

CONTACT LENSES

Neo-Flo can be used in hygienic contact lens fitting. Neo-Flo may be used to cleanse the eye of accumulated mucous and dry secretion before inserting the lens. The lens may also be washed with Neo-Flo to remove the excess cleaning and wetting agent that is used to clean the lens.

CONTAINS: Boric Acid, Sodium Chloride, Potassium Chloride, Sodium Carbonate. Preserved with Benzalkonium Chloride U.S.P. 1:15,000.

PACKAGE

Neo-Flo is supplied in a special 120 cc plastic bellows type dispenser for easy application. Gentle pressure on the base of bottle will emit a flow of solution. Flow can be controlled by varying pressure on the bottle.

PROFESSIONAL PHARMACAL CO., INC.
PHARMACEUTICAL MANUFACTURERS
300 W. JOSEPHINE ST. SAN ANTONIO, TEXAS

OCULAR

Ophthalmic Oil Suspension 1% • Ophthalmic Ointment 1%
Ophthalmic Ointment 1% with Hydrocortisone 1.5%
Ophthalmic Powder (Sterilized 25 mg., with sodium chloride 62.5 mg., and sodium borate 25 mg.)

ACHROMYCIN®

Tetracycline Lederle

a standard in local antibiotic therapy

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

modern pharmaceutical adjuncts for the office . . . to promote SIMPLICITY AND CONVENIENCE IN THE SUCCESSFUL CONTACT LENS PRACTICE

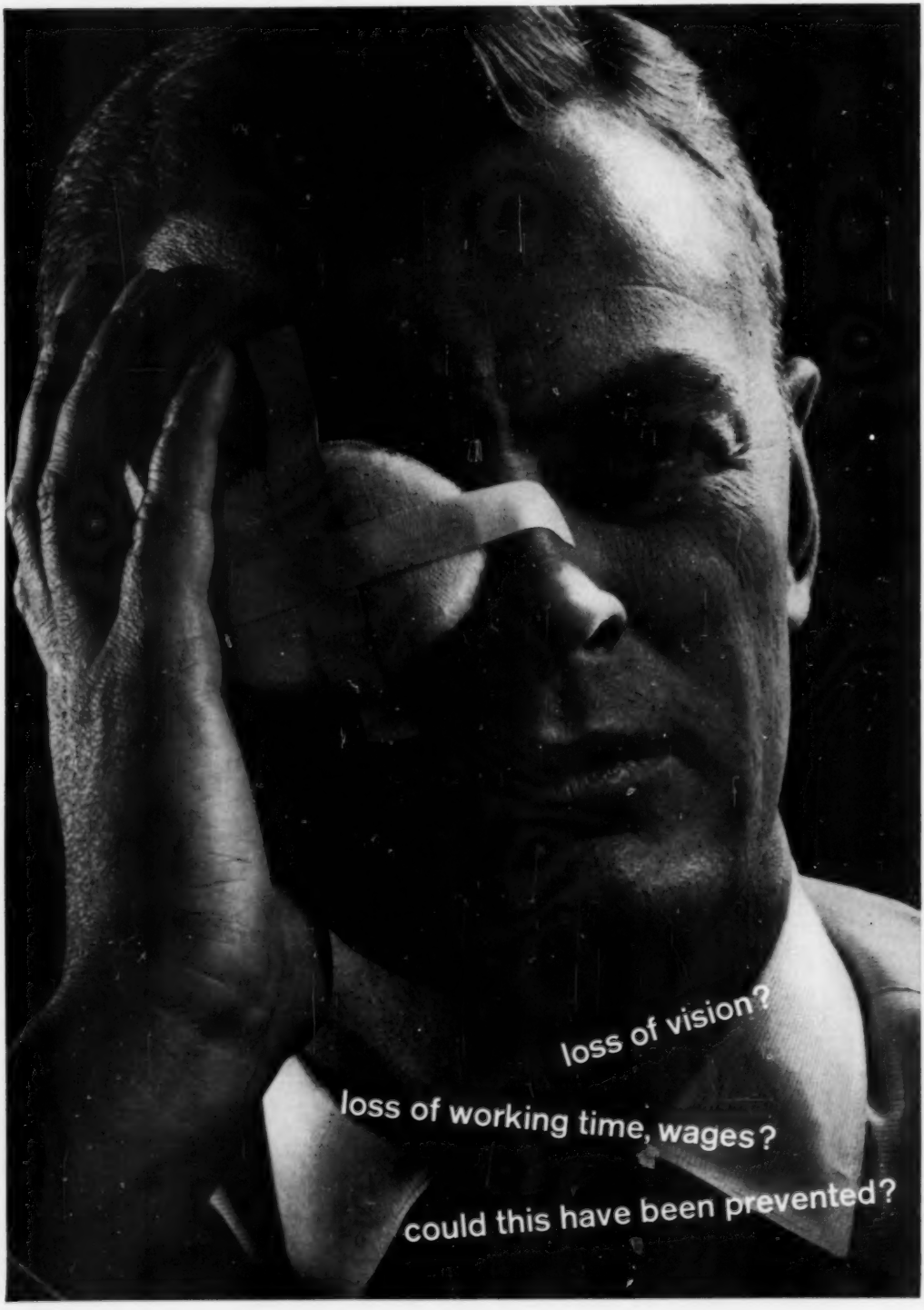
✻ **MINIMS COTTON TIP by Barnes-Hind**
(Sterile Fluorescein Sodium 2%)
Convenient, safe, sterile . . . each Minims unit is a disposable applicator for single-patient use. No need for sterilized cutting instruments. Supplied in containers of 20 individually over-wrapped Minims units.

✻ **BLINX by Barnes-Hind**
(Sterile, solubilizing irrigation solution)
Safe and non-irritating to ocular tissues because it is preserved with phenylmercuric acetate, which is completely compatible with sodium fluorescein. Solubilizes sodium fluorescein optimally because it is buffered to the alkaline pH of 8. Eliminates the incomplete solubilization of the dye crystals from fluorescein paper strips. Supplied in plastic bottles with pre-punctured tips . . . in tamper-proof containers.

✻ **NO ION by Barnes-Hind**
(Non-ionic hand cleanser for contact lens practitioners and wearers)
Free from soaps, oils, fats, and harmful detergents. Eliminates transfer from the fingertips to lens surfaces of residual soaps, cosmetics, hair lotions and skin oils—which are not removed by ordinary soaps. Does not interfere with the wettability of lens surfaces. Four-ounce plastic bottles.

All these modern office adjuncts to contact lens practice are available from contact lens manufacturers and optical wholesalers. Manufactured by the makers of Barnes-Hind Wetting Solution, Soquette Solution, and Degest ocular decongestant . . .

✻ **BARNES-HIND OPHTHALMIC PRODUCTS**
895 Kifer Road, Sunnyvale, California


loss of vision?
loss of working time, wages?
could this have been prevented?

BAUSCH & LOMB ASKS:

"why not every lens a protective lens?"

Yesterday's luxuries become today's necessities. That's how progress is made.

Perhaps today it should be as proper for a practitioner to recommend impact resistant ophthalmic lenses in every pair of glasses as it is for him to prescribe the glasses in the first place.

There are literally thousands of rulings on state and local statute books which we now take for granted, but which were put there to protect us from careless acts and from shortcomings of equipment and materials which might endanger health, life and limb. Insurance company records show such rulings are usually sound. They benefit all—maker and user, merchant and customer, doctor and patient.

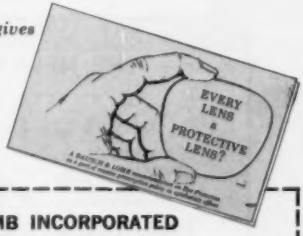
Bausch & Lomb has pioneered the field of eye safety. Out of these studies have come three advanced products which afford many times the security of ordinary dress lenses.

1. *Toughening service for regular Orthogon dress lenses of a nature vastly superior to that of years past.*
2. *"Industrial Thickness" (3 mm) lenses, for use in occupations involving constant eye hazard.*

3. *Enduron allyl ester plastic lenses—which have the added advantage of lightness.*

Your B&L Supplier is prepared to demonstrate the impact resistance as well as the optical properties of all these lenses. Your inquiry will be most welcome.

This 16-page folder gives a full account of our recommendation on eye protection. Mail this coupon for your free copy.



BAUSCH & LOMB
SINCE 1853

Made in U.S.A. by the makers of quality eyewear, Ray-Ban Sun Glasses, Balomatic Projectors, scientific instruments, binoculars, microscopes, rifle sights

BAUSCH & LOMB INCORPORATED
91113 Lomb Park
Rochester 2, New York

Please send me a copy of your brochure "Every Lens a Protective Lens"—B-1212.

Name .....

Address .....

City ..... Zone ..... State .....

THE Allied STRABISMOMETER

and Basic Fusion Trainer

Quick-Easy Diagnosis

Effective with children as young as 3 years of age!

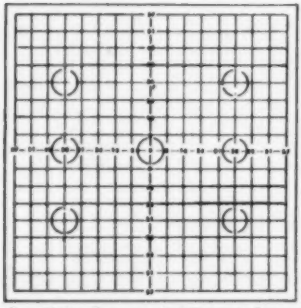
As an orthoptic instrument, the strabismometer functions to stimulate fusion at the angle of deviation, thereby enabling the doctor to prescribe pre-surgical orthoptics on a home therapy basis.

THE ALLIED RECTANGULAR CO-ORDINATE TANGENT SCREEN

The Allied One Meter Compensated Tangent Screen is calibrated in prism diopters and is the only rectangular co-ordinated screen which compensates for the increased distance between the patient's eyes and the screen, when the patient is required to fixate in the various cardinal positions of gaze. This factor is especially valuable in the diagnosis of non-comitant strabismus and heterophoria.

Screen is calibrated in prism diopters which eliminates the conversion from degrees to prism diopters.

Calibrations on screen recording charts are compensated to give accurate measurements at all positions on the screen.



One Meter Compensated Tangent Screen

Complete kit consists of: 2 hand projectors · transformer · red and green spectacles · instruction manual **$60.00**

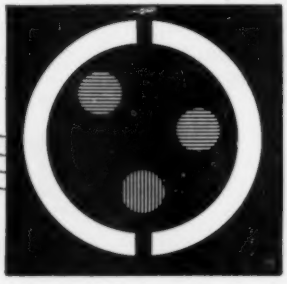
54 in. Screen and Roller, Pad of Recording Charts $20.00 additional. Sturdy Carrying Case Available $9.00 additional.

THE NEW RING FUSION TEST

Rapid efficient post-surgical test of peripheral fusion at all distances . . .

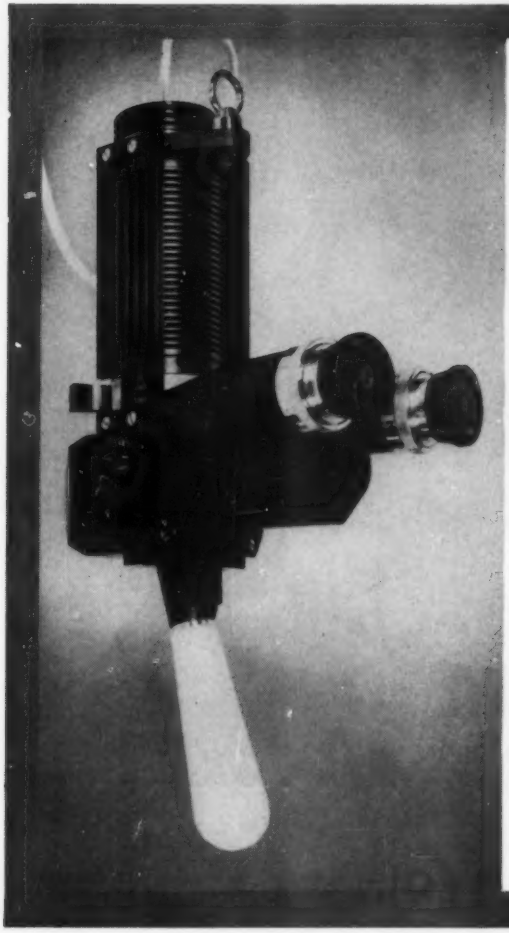
$23.50

complete with red or green goggles.



See this STRABISMOMETER and also the "New Muscle Survey Tester" by Allied in our INSTRUMENT DEPARTMENT.

The House of Vision Inc. 137 NORTH WABASH CHICAGO 2, ILLINOIS



JUST RECEIVED!

newest model
of well known

HEINE GONIOSCOPE
Now with UV filter

In our opinion this is the finest Gonioscope on the market. It's easier to handle, has better, more brilliant illumination.

- Prefocused, brilliant, air cooled light source.
- Precision German optics—10 times magnification.
- Rotating slit with easy finger-tip control.
- Adjustable P. D.
- Modern design engineered for superb performance.

AVAILABLE FOR IMMEDIATE DELIVERY!

Heine Gonioscope (as illustrated) Catalog No. HE 4001 **$365.00***

Heine Gonioscope complete with pulleys, counterweight and nylon cord, Catalog No. HE 4002 **$390.00***

** Prices include 5 amp. 6 volt transformer.*

The House of Vision Inc.

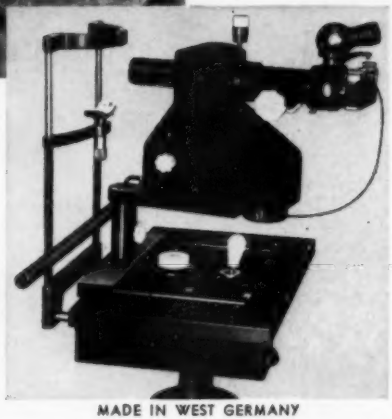
137 NORTH WABASH • CHICAGO 2, ILLINOIS

Taken with Fundus camera and 2× magnification attachment

CARL ZEISS

FUNDUS CAMERA

For magnified photographs of the fundus



MADE IN WEST GERMANY

This camera produces a picture of the fundus magnified 2½×, and covering a field corresponding to an angle of 30°. With a new 2× magnification attachment, this area can be further enlarged, producing a picture 5× natural size. This picture fills the entire frame of standard 35mm film.

Write for literature

The use of electronic flash of high intensity permits very short exposure time, eliminating difficulties caused by eye movement. Six different-shaped diaphragms permit illumination to be controlled according to the size of the patient's pupil. The newly devised telecentric light path provides a constant image magnification independent of the ametropia or accommodation to the patient's eye or of the doctor's. A compensating device, arranged in the path of rays, corrects any astigmatism continuously up to ±20 diopters.

CARL ZEISS, INC. COMPLETE SERVICE FACILITIES

485 FIFTH AVENUE, NEW YORK 17, N. Y.

EYES RIGHT

RIGHT because Gantrisin Ophthalmic Solution promptly and effectively controls a broad front of micro-organisms, including such common pathogens as *Hemophilus influenzae* (Koch-Weeks). There is little likelihood of bacterial resistance emerging. **GANTRISIN OPHTHALMIC SOLUTION** is stable, sterile and isotonic, buffered at the pH of tears...no stinging, no burning. **RIGHT** in common external eye disorders, such as "pink eye" and nonspecific conjunctivitis, punctate and dendritic keratitis, superficial corneal ulcers, blepharitis; *also* in ocular trauma, for prophylaxis following surgery and after removal of foreign bodies.

Consult literature and dosage information, available on request, before prescribing.

Gantrisin Diethanolamine Ophthalmic Solution and Ointment contain 4% Gantrisin●—brand of sulfisoxazole.

ROCHE
LABORATORIES
Division of Hoffmann-La Roche Inc.

℞

Memo To Ophthalmologists

LET YOUR GUILD OPTICIAN USE HIS SKILLS AND EXPERIENCE TO SERVE YOUR PATIENTS

GUILD ℞ OPTICIANS

You can send your patients to your Guild Optician with the sure knowledge that he will

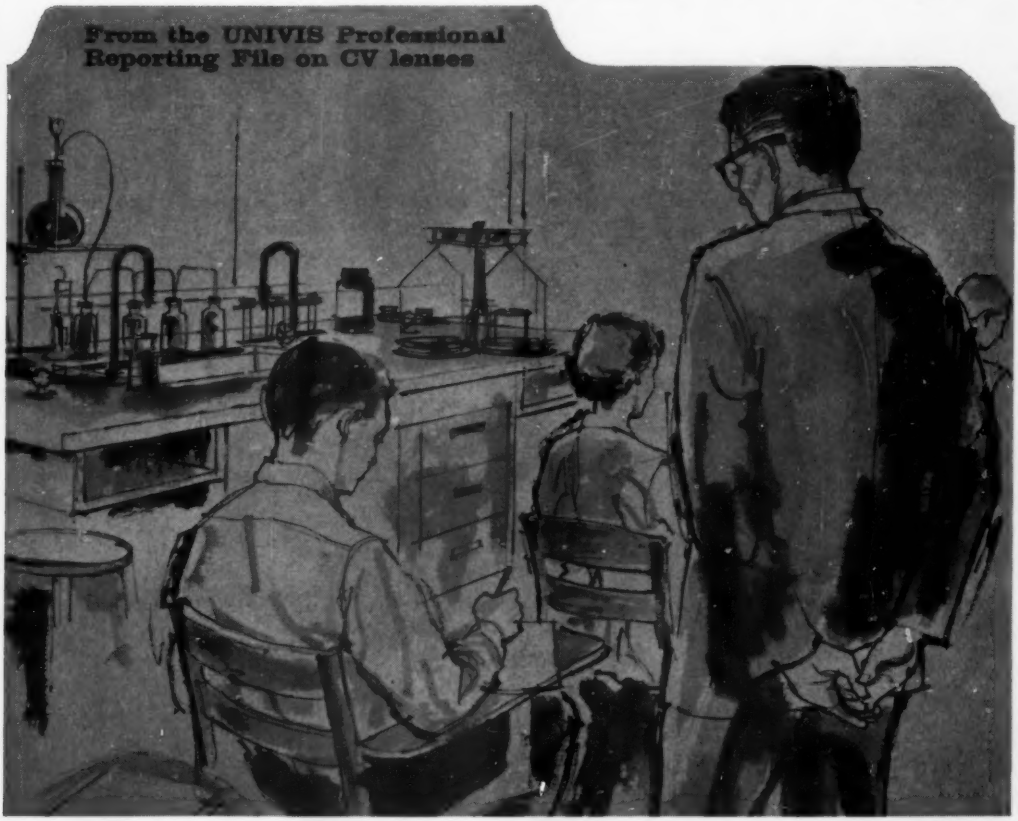
. . . accurately fill your prescription

. . . have time, experience and patience for special problems that demand frequent adjustment

. . . be always readily available for any problems of aftercare and repair for the life of the glasses

. . . use his skill and experience to help you and your patients.

Guild of Prescription Opticians of America, Inc.
110 East 23rd Street, New York 10, New York



"A physics teacher said he could walk down aisles and see students' papers without leaning over and breathing down students' necks"

That's what one presbyope told his doctor . . . with his youthful vision restored, permitting him to see clearly in all ranges, near, intermediate, and distance. For many such patients with a reading add above 1.75 D., Univis CV* lenses are *the* satisfaction Rx. Help build practice, too. We'd like to hear of *your* experiences.

more than 2 MILLION **UNIVIS** *CV lenses prescribed*

*T.M./UNIVIS Inc.

SIMMAY
ELECTRIC OPHTHALMOSCOPE
with test for the diagnosis
of monocular eccentric fixation

COCHET & BONNET
AESTHESIOMETER
for measurement
of corneal sensibility

Prompt delivery
Write for
literature and quotation

TARLE
ELECTRIC SKIASCOPE
with rectilinear spot
Totally free from any reflection
Direct pupillary shifts
in any case of refraction

BEYNE INSTRUMENTS
OPTOMETER
SCOTOPTOMETER
CHROMOPTOMETRIC LANTERN
for estimation men's aptitude to various operations as in Industrial Work, Army, Navy, Aircraft, Railways, etc.
Complete information available on request

LUNEAU & COFFIGNON
ophthalmic instruments
3, RUE D'ÉDIMBOURG - PARIS 8E - FRANCE

A new Jenkel-Davidson design

SELECTACHART

No place for your projector?
The new Jenkel-Davidson
Selectachart gives remote
control so you can mount your
projector as much as five feet
from your trial lens cabinet
or other control center.
Priced at only **$325**
including projector.

Write for complete information, no obligation

Jenkel-Davidson
OPTICAL COMPANY
366 Post St., San Francisco, California

new!

stable, sterile, non-irritating
epinephrine ophthalmic solution

GLAUCON

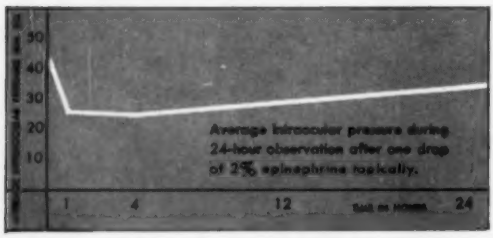
for chronic, open-angle glaucoma

Garner, et al., recently studied the effects of GLAUCON Ophthalmic Solution (epinephrine HCl 2% in a new stable vehicle) on intraocular pressure in open-angle glaucomatous eyes. GLAUCON proved to be so highly effective that the investigating group summarized[1]:

"GLAUCON has a valuable place in the medical armamentarium of the ophthalmologist . . ." and, "it has specific advantages in the treatment of open-angle glaucoma since it rarely produced intolerance in almost three years of observation."

the results with GLAUCON *were reported[1] as follows:*

1 "The topical application of 2% epinephrine [GLAUCON] to 44 glaucomatous eyes under no other therapy and of the chronic, simple type results in a drop in the intraocular pressure ranging from 3 mm. Hg to 38 mm. Hg with an average of 13.5 mm. Hg."



2 "The removal of epinephrine [GLAUCON] topical therapy from 43 eyes previously stabilized and normalized on combined therapy [GLAUCON and a miotic] and permitted to be without this medication for a period of seven days results in a rise in the intraocular pressure ranging from 4 mm. Hg to 31 mm. Hg with an average rise of 11.7 mm. Hg. It is in this group that the greatest number of satisfactory results were noted . . ."

"The patient that is difficult to normalize on miotics and who remains in the vicinity of the mid-to-upper twenties tends to reveal the best results, insofar as the tension can now be easily maintained in the low or below twenties on one or two applications of epinephrine [GLAUCON] per day. As a result, this type of patient has been able to reduce the frequency of miotic therapy so that in some instances medication need no longer be carried, since morning and evening application of both miotic and 2% epinephrine [GLAUCON] was sufficient."

3 "Of the entire total of 219 eyes in this series, 69, or 31%, were not controlled by any means, while 21 (9.5%) were controlled on epinephrine [GLAUCON] alone and 54 (24.6%) more by combined miotic and epinephrine [GLAUCON] and an additional 35 (15,9%) when a carbonic anhydrase inhibitor was added."

Since miotics alone controlled 40 (18.2%) eyes, GLAUCON effectively aided or controlled tension in 61% of all eyes in which it was used. It controlled or helped control 79% of chronic, simple (open-angle) glaucomatous eyes.

4 "Tonographic studies gave evidence that the best results (91%) in significantly lowering intraocular tension occurs in those cases whose coefficient of outflow is 0.15."

5 Dilatation of the pupil was noted in all patients not under miotic therapy. Two patients had orbital pain which remained for about two hours. Two other patients developed marked hyperemia associated with moderate epiphora but these disappeared promptly after withdrawal of epinephrine.

GLAUCON has been proven to be effective in normalizing chronic, simple, open-angle glaucoma. In cases resistant to miotic therapy it effectively reduces tension alone or when combined with the miotics. Suggested dosage is one drop in eye(s) per day or as indicated.

Use and prescribe GLAUCON in your practice. GLAUCON is supplied in sterile, 10 ml. bottles with a sterile dropper assembly. All drug wholesalers now have GLAUCON in stock. Your pharmacist can supply it promptly.

GLAUCON CAUSES LITTLE IF ANY PAIN OR STINGING UPON APPLICATION. CLINICAL EXPERIENCE CONTINUES TO DEMONSTRATE HIGH PATIENT ACCEPTANCE AND GENERAL AVOIDANCE OF DISCOMFORT.

1. Garner, L. L.; Johnstone, W. W.; Ballintine, E. J.; and Carroll, M. E.: Effect of 2% Levo-Rotary Epinephrine on the Intraocular Pressures of the Glaucomatous Eye. A.M.A. Arch. Ophth. 62:230 (Aug.), 1959.

haug
DRUG CO.
4905 N. 31ST STREET
MILWAUKEE 9, WIS.

LONG TERM IODIDE THERAPY WITHOUT IODISM

YOU can prescribe Iodo-Niacin in full dosage for a year or longer *without any danger of iodism.*[1]

Iodo-Niacin tablets contain potassium iodide 135 mg. with *protective* niacinamide hydroiodide 25 mg. Recommended dosage, 2 tablets three times a day.

The *principal indications* for Iodo-Niacin include arteriosclerosis[1], bronchial asthma, chronic bronchitis[2], simple colloid goiter, sinusitis[2], retinal or vitreous hemorrhages[3], and vitreous floaters.[3]

In *emergencies,* Iodo-Niacin ampuls are available for intramuscular or intravenous injection.[4]

Iodo-Niacin® tablets, slosol coated pink, are supplied in bottles of 100. Ampuls 5 cc. in boxes of 10.

IODO-NIACIN*

TABLETS AND AMPULS

1. *Am. J. Digest. Dis.* 22:5, 1955.
2. *Southwestern Med,* 40:120, 1959.
3. *Am. J. Ophth.* 42:771, 1956.
4. *M. Times* 84:741, 1956.

U.S. Patent Pending

Cole CHEMICAL COMPANY
3721-27 Laclede Avenue
St. Louis 8, Mo.

COLE CHEMICAL COMPANY AJO-1
3721-27 Laclede Ave., St. Louis 8, Mo.

Gentlemen:
Please send me professional literature and samples of IODO-NIACIN.

..... M.D.

..... Street

City ..... Zone ..... State .....

4 ophthalmic products with distinctive advantages...

- their wide-spectrum bactericidal activity includes *ALL clinically isolated strains of Pseudomonas aeruginosa*, a serious invader noted for the rapidity of its destructive powers.
- their component antibiotics rarely sensitize.

NEW

'CORTISPORIN'® brand
OPHTHALMIC SUSPENSION
Polymyxin B-Neomycin with 1% Hydrocortisone

Available in bottles of 5 cc. with sterile dropper.

'CORTISPORIN'® brand
ANTIBIOTIC OINTMENT
Polymyxin B-Bacitracin-Neomycin with 1% Hydrocortisone

Available in ⅛ oz. ophthalmic tubes.

'NEOSPORIN'® brand
ANTIBIOTIC OPHTHALMIC SOLUTION
Polymyxin B-Gramicidin-Neomycin

Available in bottles of 10 cc. with sterile dropper.

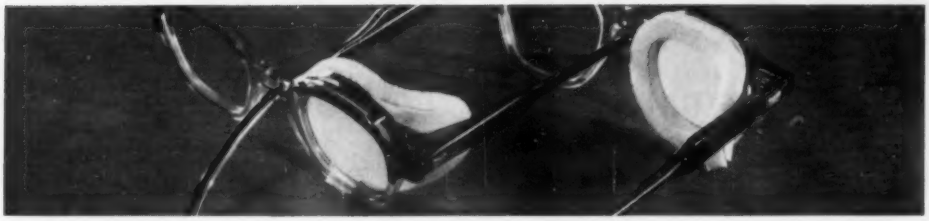
'NEOSPORIN'® brand
ANTIBIOTIC OINTMENT
Polymyxin B-Bacitracin-Neomycin

Available in ⅛ oz. ophthalmic tubes.

Complete information available on request.

BURROUGHS WELLCOME & CO. (U. S. A.) INC., Tuckahoe, New York

NEW! cushioned, ventilated, blackout, OCCLUDER by PAP



Available in black or white

Cushioned Flexibility—New sponge latex edging gently hugs facial contours completely blocking out vision.

Comfortable and Sanitary—Can be worn all day with complete comfort due to cushioned, ventilated edging. Is washable.

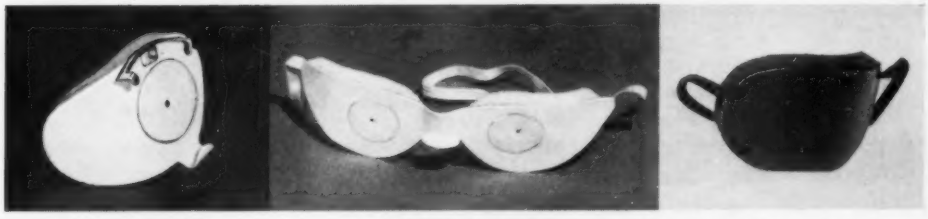
Easy to Attach—The three sizes will fit all types of frames. Will not loosen or fall off. Can be removed easily.

Ventilated—Soft porous edging permits circulation of air thereby reducing perspiration.

Available in three sizes
with carrying case (right or left)
$2.25 each, $1.95 in doz. lots
Pinhole $2.50 ea. & $2.25 in doz. lots

SMALL—Fits frames 34 or 36
MEDIUM—Fits frames 38 or 40
LARGE—Fits frames 42 or 44

ALSO NOW AVAILABLE FROM PAP!



Pinhole Eye Occluder **Double Pinhole Eye Cover** **Single Eye Cover**

Order through your supplier or direct

Pap

PERM-ADJUST PAD COMPANY, CHICAGO 47, ILLINOIS
PHONE Di 2-2886

ABC

brings you a
new addition to our

STRAIGHT TOP MULTIFOCAL FAMILY

with exclusive

GITSON PROCESS

ACCURACY...

Volk CatraConoid Bifocals

Aspheric Cataract Lenses in GLASS

***NOW** Your Aphakic Patients Can Have Clear*
Side Vision to: Park easily... Use the mirror...
Read comfortably... Walk confidently... Work efficiently

Post-operative Adaptation to Cataract Lenses
is Faster with Volk CatraConoid Bifocals

- No telltale bull's-eye circle
- Clear, edge-to-edge distance vision
- Clear, wide-field, deep-focus reading vision

Manufactured Exclusively by American Bifocal Co., Inc.
Under the GITSON PROCESS

ABC
GITSON PROCESS

AMERICAN BIFOCAL COMPANY, INC.

Producers of Straight Top ABC Bifocals and Trifocals
For Every Purpose

1440 ST. CLAIR AVENUE • CLEVELAND 14, OHIO

ACTIVITIES LIKE THESE CALL FOR...

SPORTS

ATHLETICS

INDUSTRY

CHILDREN'S PLAY

GLASS GARD

the safe, comfortable eyeglass holder

- Perfect for athletic, industrial and children's wear. Guards against accidental dropping and breakage.
- Elastic fits snugly but comfortably – keeps glasses firmly in place.
- Adjusts easily to all head sizes.
- May be attached and removed quickly and easily without damaging frame.

PRICE/$7.50 per dozen, retail
(minimum order, 1 doz.)

ORDER FROM YOUR OPHTHALMIC SUPPLY HOUSE OR . . .

Precision-Cosmet Company, Inc.

529 SOUTH SEVENTH STREET
MINNEAPOLIS 15, MINNESOTA

PRECISION-COSMET COMPANY, INC. Dept. A-11
529 South 7th Street • Minneapolis 15, Minn.

Please rush_____doz. GLASS-GARD eyeglass holders.

Name_____

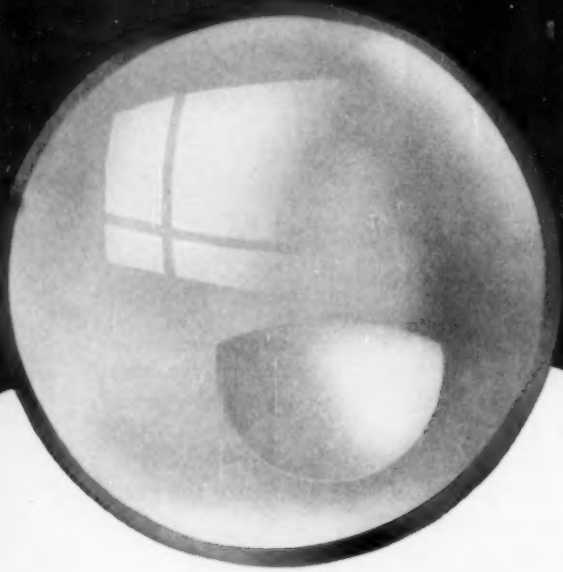
Address_____

City_____ **Zone**____ **State**_____

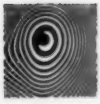
Name of Supplier_____

MARK OF DISTINCTION ...IN MULTIFOCALS

AO SOVEREIGN LENS



with the segment that follows the natural sweep of the eye



Many people—by virtue of their everyday activities or personal tastes—prefer something *more* than an ordinary bifocal. And, in the Tillyer SOVEREIGN they find it. For, unlike conventional multifocals, the segment top of the Tillyer SOVEREIGN is *curved*—to follow the natural sweep of the eye and to offer a generous, comfortable area for near-vision tasks. This distinctive curved top is also highly effective in reducing reflections . . . often a source of annoyance in other bifocal and trifocal lens designs. When prescribing a multifocal lens, why not offer your patients the truly distinctive AO SOVEREIGN. Available in 20, 22 and 25 mm segments through your local AO Branch or Franchised Distributor.

American Optical COMPANY

SINCE 1833...BETTER VISION FOR BETTER LIVING

AMERICAN JOURNAL OF OPHTHALMOLOGY

SERIES 3 · VOLUME 51 · NUMBER 1 · JANUARY, 1961

CONTENTS

COLOR PLATES

Illustrating paper by Edward G. Fortier ..... *facing pages* 108-111
Illustrating paper by Maxwell Thomas and Ronald M. Burnside ..... *facing page* 142

ORIGINAL ARTICLES

The development of ophthalmic anesthesia: The Sanford R. Gifford Lecture. Walter S. Atkinson 1
Mistaken diagnoses in some cases of meningioma: Clinics in Perimetry No. 5. C. Wilbur Rucker and Thomas P. Kearns 15
Uveitis: III. Peripheral uveitis: Pathogenesis, etiology and treatment. R. J. Brockhurst, C. L. Schepens and I. D. Okamura 19
Cataract extraction with the modified Smith technique. Richard A. Ellis 26
Familial retinal detachment. A. I. Friedmann and E. Epstein 33
Methods for the separation of lids in cataract surgery. Paul U. Fechner 35
The inactivation of herpes-simplex virus by chemical agents. Theodore W. Sery and Francis P. Furgiuele 42
An evaluation of heparin in the treatment of senile macular degeneration. Norman F. Schwilk, Jr., and Alan J. Rosenberg 57
Episcleral nodules and erythema nodosum: Report of a case with the pathologic findings. James L. McCarthy 60
Scleromalacia perforans and massive granuloma of the sclera: A report of an unusual combination of ocular pathology in rheumatoid arthritis. J. Reimer Wolter and Maxwell D. Bentley 71
Eye protection against small high-speed missiles. George M. Stewart 80
The localization of Diamox-S^{35} in the rabbit eye. Seymour B. Goren, Frank W. Newell and John J. O'Toole 87
A history of Philippine ophthalmology. Geminiano de Ocampo 93
Chymotrypsin in various ophthalmic surgical procedures. Wendell L. Hughes, Earl L. Lewis and Joseph Amdur 103
Use of intramuscular chymotrypsin in controlling tissue reaction following strabismus surgery: A preliminary study. Edward G. Fortier 106
An experimental investigation of the basic phenomena of retinopexy: III. Resistance and capacitive reactance of the cat's cornea, sclera, choroid and vitreous. Henry A. Knoll .. 113
The use of absorbable sutures in surgery of the cornea. Samuel D. McPherson, Jr. 118
Von Hippel-Lindau disease. Maxwell Thomas and Ronald M. Burnside 140

NOTES, CASES, INSTRUMENTS

Alpha chymotrypsin in intraocular foreign body extraction. Henry L. Hilgartner and Hardy E. Thompson, Jr. 147
Posterior embryotoxon: Report of an interesting case. Frederick C. Wuest and Wayne L. Erdbrink 148
Scleral rigidity determinations: Before and after tonography. J. William Rogers and Winston Roberts 150
Bilateral nuclear ophthalmoplegia: Report of a case with cerebellar symptomatology. R. Douglas Collins 152
Pigmented papilloma of the limbus: Undergoing malignant change. B. M. Chatterjee 154
Frequency of sympathetic ophthalmia: In different parts of the world. Adalbert Fuchs ... 156
An eye-dressing tray. Y. A. Staton 158

OPHTHALMIC RESEARCH

Abstracts of papers presented at the meeting of the Mid-Southern Section of the Association for Research in Ophthalmology, Inc., Fort Worth, Texas, November 11 and 12, 1960 .. 159

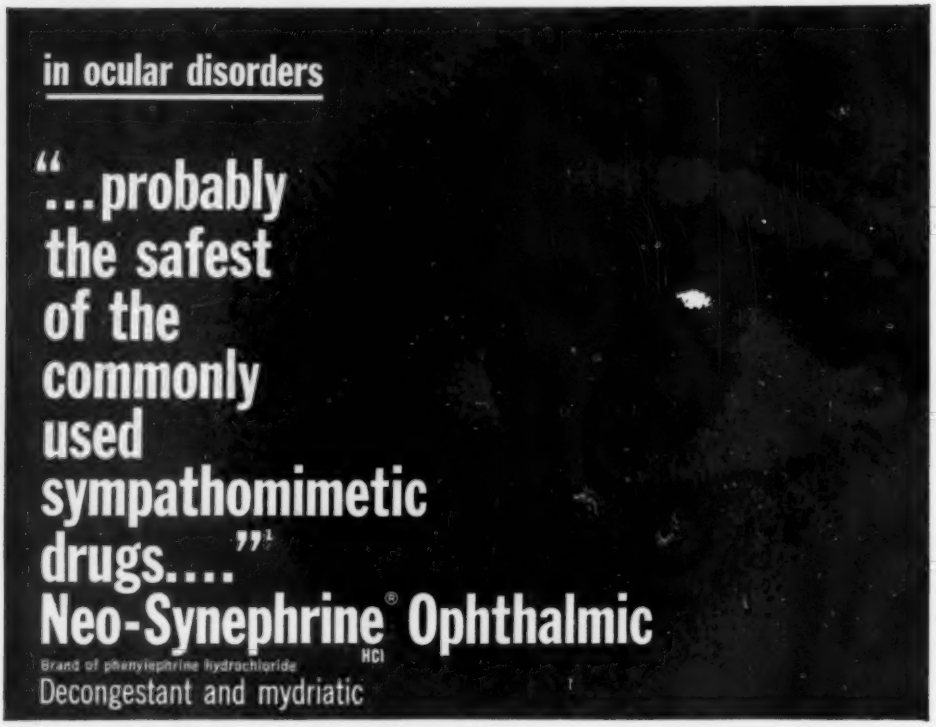
SOCIETY PROCEEDINGS

New York Society for Clinical Ophthalmology, April 6, 1959. Panel discussion on "Ocular physiology in clinical practice" 161

EDITORIALS

Asia-Pacific Academy of Ophthalmology 178
Congress of the Japanese Ophthalmological Society 180

(Continued on page 216)


in ocular disorders
"...probably the safest of the commonly used sympathomimetic drugs...."[1]
Neo-Synephrine® HCl Ophthalmic
Brand of phenylephrine hydrochloride
Decongestant and mydriatic

Neo-Synephrine Ophthalmic in dilute solution (⅛ per cent) has a mild decongestive effect without causing appreciable mydriasis. Stronger solutions produce a prompt and short-acting mydriasis that is almost entirely free from cycloplegia. Nontoxic in therapeutic doses, Neo-Synephrine Ophthalmic does not produce unpleasant or alarming side reactions, lose effectiveness on repeated administration or cause compensatory vasodilatation after vasoconstriction.

The low surface tension of the emulsion and the aqueous vehicles permits prompt, uniform spreading over the entire conjunctival surface.

Five dosage forms provide wide application in ophthalmology. All are available in glass bottles with dropper and, except for the emulsion, in Mono-Drop® squeeze bottles that eliminate dropper contamination and simplify instillation.

⅛ per cent solution. Decongestive collyrium for rapid relief of burning, itching and smarting.

2.5 per cent solution. For short-acting mydriasis in refraction, ophthalmoscopy, surgery and in provocative test for angle block in glaucoma.

10 per cent solution (plain or viscous) and emulsion. For rapid powerful mydriasis and decongestion. In uveitis: with atropine, for freeing recently formed posterior synechiae and preventing their formation. In glaucoma: for temporarily reducing intra-ocular tension. For use in surgery.

1. Gordon, D. M.: **Am. J. Ophth.** 47:536, April, 1959.

Winthrop LABORATORIES
New York 18, N.Y.

Neo-Synephrine (brand of phenylephrine), and Mono-Drop, trademarks reg. U. S. Pat. Off.

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 51 JANUARY, 1961 NUMBER 1

THE DEVELOPMENT OF OPHTHALMIC ANESTHESIA*

THE SANFORD R. GIFFORD LECTURE

WALTER S. ATKINSON, M.D.
Watertown, New York

I am indeed honored to be asked to deliver the Gifford Memorial Lecture this year. Dr. Gifford (fig. 1) was a greatly admired colleague and I treasure the thought that he was a good friend. He was an outstanding ophthalmologist, an eminent scholar, a charming companion with a delightful sense of humor who was greatly loved by his many associates and friends. To enumerate Dr. Gifford's many accomplishments to you here in Chicago would indeed be "carrying coals to Newcastle."

A subject dealing with anesthesia was chosen for this occasion because it is one which has interested me for many years and also because Dr. Gifford evinced so much interest in my candidate's thesis on anesthesia for the American Ophthalmological Society.

In the preparation of this lecture I have been impressed with the frequency with which there is an interval of many years after an important observation or discovery has been reported before it is adopted by the medical profession.

Possibly the answers to some of our unsolved problems in ophthalmology could be found in observations lying dormant in our minds and in ophthalmic or general medical literature, if we were alert to recognize and adopt them.

In reviewing the development of anesthesia, early accounts indicate that little success was achieved in preventing the pain of surgery during the 2,000 years prior to 1846 when the anesthetic property of ether was first demonstrated to the medical profession.

In the ophthalmic portion of the *Tetrabiblion of Aëtius of Amieda,* there is no reference to the prevention of pain for surgical operations. The ancients apparently relied principally upon stalwart assistants in lieu of anesthesia to secure a quiet, if not a relaxed, patient. That the patients were not always quiet is evident from a remark of Aëtius, that care must be observed in the operation for pterygium to avoid cutting the lids.

SLEEP SPONGES (SPORGIA SOMNIFERA)

In medieval times the spongia somnifera or sleep sponges, which contained narcotics, were popular and, according to the account in the *Antidotarium of Nicolaus Salernitanus,* they effectively produced sleep. However, they were discontinued because if large enough doses were used to produce narcosis, they were dangerous to life, and small doses were not effective. Also, as indicated in the *Bibliotheca Osleriana,* they were abandoned because of the introduction of the tourniquet to prevent pain of amputations which were the most common operations in those days.

EARLY LOCAL ANESTHETIC AGENTS

The early Egyptians are said to have rubbed the powdered skin or fat of a crocodile upon the patient's skin to produce local anesthesia. According to Plineus and Dioscorides, the Memphitic Stone of Egypt mixed with vinegar produced local anesthesia when it was rubbed on the patient's skin. The various methods advocated to produce local anesthesia over the years were tried by

* Presented at the Clinical Conference of the Chicago Ophthalmological Society, February, 1960.

Fig. 1 (Atkinson). Sanford Robinson Gifford, M.D.

enthusiastic followers and usually discarded since others probably lacked the hypnotic ability of those who advocated the method.

Hypnosis or suggestion, intentional or unintentional, has undoubtedly played a more important part than is generally realized in the success of many types of therapy. Even the popular double-blind technique of testing drugs is influenced by the individual who administers the drugs.

The general effect of chewing coca leaves has been known for centuries. Moodie[1] depicts a prehistoric surgical operation in Peru in which the surgeon is said to have in his cheek a quid of coca leaves which he applied to the wound to ease the pain. This suggests that the local effect was also appreciated.

Hypothermia

About the middle of the 17th century, Severino and Bartholinus, a Danish student of Severino, advocated cold as a means of producing anesthesia.[2] It is still used to some extent and, during recent years, there have been interesting advances in the use of hypothermia to produce anesthesia.

Ether and Nitrous oxide

It is difficult now for us to appreciate the terror experienced by the patients and their heart-rending shrieks during an operation performed without anesthesia, yet this was the case just a little over 100 years ago. Speed and imperturbability were essential assets of the surgeon in preanesthetic times. Prior to the advent of anesthesia, comparatively few operations were done. For example, at the Massachusetts General Hospital,[3] during the five years preceding the introduction of anesthesia by Morton, there was an average of only three operations a month. Most patients preferred to die rather than suffer the agonizing pain and shock of an operation. Surgeons also dreaded the ordeal of operating upon a screaming and struggling patient. For these reasons, not many doctors cared to do surgery or even witness operations.

In the year 1800, Humphrey Davy[4] described the anesthetic properties of nitrous oxide and suggested its use for surgical operations. This suggestion was overlooked or went unheeded for over 40 years before its adoption, as has been the case with many other good suggestions.

Horace Wells, in 1844, used nitrous oxide to extract teeth without causing pain. An unfortunate set of circumstances led to Wells' failure to demonstrate successfully the anesthetic property of nitrous oxide in January, 1845, at the Massachusetts General Hospital. This was not only unfortunate for Wells but for patients who must have suffered needlessly the agony of an operation without anesthesia before the successful demonstration of ether almost two years later at the same hospital.

It is now well known that Long, in 1842,[5] had used ether on several occasions to prevent the pain of operations but he failed to make it known to the medical profession so the credit is usually given to Morton. As Darwin[6] said: "In science the credit goes to the man who convinces the world, not to the man to whom the idea first comes."

The administration of ether by Morton (fig. 2) at the Massachusetts General Hospital, in 1846, for the removal of a tumor which was done without causing pain was

Fig. 2 (Atkinson). Morton's demonstration of ether anesthesia at the Massachusetts General Hospital.

electrifying news which spread rapidly over the world. It is interesting to note that ether was known to chemists and physicians as early as 1450, yet it was almost 400 years before its anesthetic property was accidently discovered. It is really amazing how much lies dormant for years before its value is appreciated and adopted. One wonders if we are overlooking some obvious etiologic factors or methods of preventing or treating such diseases as glaucoma?

Hypodermic needle

The hollow needle, which was devised by Alexander Wood[7] in 1853, made it possible to inject anesthetic drugs to produce anesthesia when the first local anesthetic agent, cocaine, was introduced over 30 years later. Before the discovery of local anesthetic agents, repeated attempts were made to produce local anesthesia by the injection of sleep-producing drugs which obviously resulted in failure.

Cocaine

Gaedcke,[8] in 1855, was the first to discover the alkaloid of the coca leaves (*Erythroxylon coca*) and called it erythroxylin but his report was apparently overlooked. Five years later, in 1860, Neiman[9] isolated the powerful alkaloid of the coca leaves which he named cocaine. In describing it he said that it "benumbs the nerves of the tongue, depriving it of feeling and taste." The same year Scherzer[10] noticed that on chewing the coca leaves it caused a feeling of numbness of the tongue.

In 1879 von Anrep[11] investigated the local action of cocaine upon the skin and conjunctiva. He noted the anesthetic action on the skin after injecting a weak solution of cocaine but observed only the mydriatic action of the drug when it was instilled in the eye.

In 1880 Coupard and Bordereau[12] observed the loss of the corneal reflex when cocaine was instilled in the eyes of animals but their observations received little attention.

It was 30 years after the report of Gaedcke that Koller's[13] report on the use of cocaine to produce anesthesia for eye surgery was presented at Heidelberg. Apparently Koller (fig. 3) was unable to attend the meeting so a colleague read his communication and demonstrated the anesthetic effect of cocaine for eye surgery. Immediate acceptance of cocaine is evidence of the convincing manner in which it was presented. This was indeed fortunate for Koller who is usually given full credit for this outstanding advance.

Fig. 3 (Atkinson). Carl Koller, M.D.

Following Koller's report the era of modern ophthalmic surgery really began.

In December of the same year, 1884, Dr. Herman Knapp[14] (fig. 4) published a complete summary of the literature in regard to the use of cocaine in all branches of surgery in which Bull of Bellevue Hospital in New York is credited as being the first surgeon in America to use cocaine to produce anesthesia.

First retrobulbar injection

Here it is interesting to note Knapp's simple and effective method of making a retrobulbar injection to produce anesthesia of the globe for enucleation which he reported in his 1884 summary, only three months after the anesthetic property of cocaine was demonstrated at Heidelberg. It is as follows:

> Cocaine four percent was instilled, then the globe was rotated toward the nose with forceps and a needle was introduced through the conjunctiva temporally into the muscular cone just posterior to the globe and six minims of a four percent solution of cocaine were injected. The eye was then enucleated without pain.

Although others have been given the credit for introducing the retrobulbar injection, the procedure described by Knapp is the first report found in the literature.

The toxicity of cocaine was quickly realized but not until many unhappy results had followed its use, particularly in general surgery, in which larger quantities were used than in ophthalmic surgery. The fear of a toxic reaction deterred ophthalmologists from making injections to produce local anesthesia and akinesia for another 20 to 30 years. Many of the unfortunate accidents were probably caused by injecting the anesthetic solution into a vessel or to the rapid injection of strong solutions of the anesthetic which were absorbed rapidly since epinephrine had not yet been discovered.

Nerve block

The infiltration of cocaine near or into the nerve was first reported by Hall and Halsted[15] in 1884. They observed that the tissues supplied by the nerves so injected became anesthetic. This was the beginning of the important anesthetic procedure of "nerve block."

The danger of a forcible contraction of the orbicularis muscle during a cataract extraction and other eye operations had been feared for many years, yet it was not until 30 years after Hall and Halsted's report that an ophthalmologist, van Lint, in 1914,[16] thought of blocking the facial nerve to produce akinesia of the orbicularis. We are probably overlooking many measures of equal value today.

Synthetic preparation of local anesthetic agents

In 1899, the discovery of the chemical composition of cocaine and its atomic grouping by Einhorn[17] made its synthetic preparation possible. This research was the starting point of combining the anesthesiophore atomic groups with new atomic groups that led to Einhorn's discovery of procain (Novocaine) in 1905. Many other new local anes-

thetic agents were soon synthesized. We now have the choice of short, medium, or long-acting anesthetic agents. Another advantage in having a choice of many good anesthetic agents is that, if a patient is sensitive to one local anesthetic, we can change to another from the following groups: (1) benzoic acid esters—cocaine and metacaine; (2) para-amino-benzoic acid esters—(Novocaine, Pontocaine, Monocaine); (3) quinolin derivative—(Nupercaine); (4) the basic anilid—(Xylocaine).

Epinephrine (adrenalin chloride)

In 1901, Takamine[18] isolated the active salts of the suprarenal gland and added epinephrine (adrenalin chloride) to our pharmacopoeia. It was quickly learned that when epinephrine was used with a local anesthetic agent it retarded absorption, decreased the toxic effect of the agent, and lengthened the duration of the anesthesia. In addition, it has been observed[19] that when the concentration of epinephrine in retrobullbar injections is increased greater hypotony is produced.

The discovery of adrenalin chloride in 1901 and of the less toxic anesthetic agent, Novocaine, in 1905 immediately revived interest in local anesthesia. As a result, important advances developed rapidly in the methods of producing anesthesia and akinesia.

Preanesthetic preparation

Until comparatively recently little attention has been given the pre-anesthetic preparation of the patient. Some surgeons still have their patients for cataract extraction and other intraocular surgery walk to the operating table with little or no preanesthetic preparation or medication. In most hospitals, however, its advantages have been recognized and careful attention is given preanesthetic preparation.

Good sedatives, analgesics, and relaxants have greatly minimized complications and the patients' dread of an operation. With the use of these and improved local anesthesia, operations have been made safer and practically painless which allows the surgeon to carry out a deliberate and precise technique.

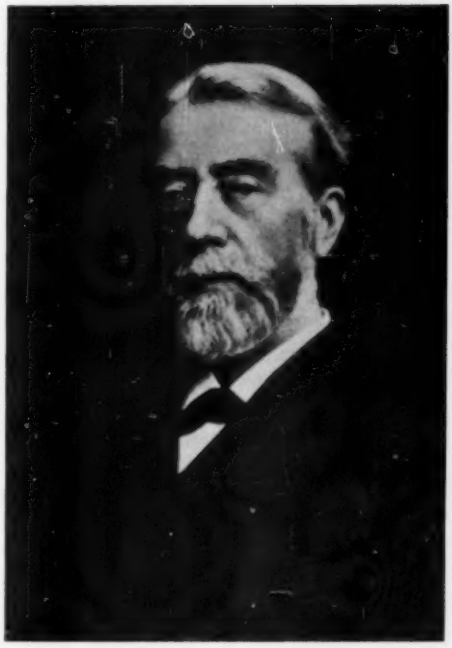


Fig. 4 (Atkinson). Herman Knapp, M.D.

I am convinced that careful preanesthetic preparation combined with good anesthesia and akinesia is responsible for saving many eyes.

A few years ago, through the courtesy of Dr. Breinin[20] and with his valuable assistance, an attempt was made to estimate by electromyography the akinesia following injections to block the nerve supply to the orbicularis muscle. Six injections that were given to patients who had had *no* preanesthetic preparation produced complete akinesia in only one.

The clinical evaluation of the paralysis was consistent with the electrical waves shown on the oscilloscope. The principle advantage of electromyography for this type of investigation, it seems to me, is that the muscle activity is graphically shown, timed, and recorded on film.

The same anesthetic and method of injec-

tion as used in the above injections were used in over 1,000 patients who had had adequate preanesthetic preparation. The paralysis of the orbicularis was clinically evaluated and was complete in all.

This added to my conviction that good preanesthetic preparation is necessary in order to obtain complete akinesia. It also convinced me that the method of injection which will be described later is effective.

The various methods of preanesthetic preparation are well known and we have all developed our own measures so a discussion of them seems unnecessary.

However, it might be emphasized that, in my opinion, a safe stage of sedation for intraocular operations is one in which the patient is amnesic, but still mentally co-operative with a feeling of unconcern in regard to the operation. I have observed more operative accidents with too much sedation than with too little. With too much the patient may be disoriented and difficult to manage. With too little, more of the sedation may be given if necessary.

Serious complications may occur due to heavy sedation after the patient returns to his bed. He may aspirate vomitus, develop respiratory arrest or damage his eye if not watched constantly. The shortage of nurses makes constant attendance difficult and recovery rooms are not always available.

Anesthetic agents

Of the various anesthetics for instillation anesthesia prior to surgery, my choice is tetracaine (Pontocaine) hydrochloride 0.5 percent. For tonometry and patients who are sensitive to tetracaine, benoxinate hydrochloride (Dorsacaine) 0.4 percent is my choice.

For injections my preference is lidocaine (Xylocaine) hydrochloride two percent with the addition of epinephrine 1:50,000 or 1:100,000, unless epinephrine is contraindicated. To this is added hyaluronidase six turbidity reducing units to each cc. to cause greater diffusion of the anesthetic solution, thus producing more complete anesthesia and akinesia. When hyaluronidase is added to the anesthetic solution for retrobulbar injections, more marked hypotony is obtained.[21]

In spite of reports to the contrary, the duration of the anesthesia is decreased very little by the addition of hyaluronidase to the anesthetic solution if it contains epinephrine and the patient has had adequate preanesthetic preparation. It has been my experience that the anesthesia lasts considerably longer than most eye operations.

Syringes and needles

Improved syringes with locks to prevent the needle from popping off during the injection and rustless steel needles have added greatly to the ease of making the injection.

A complication that should be remembered is the tissue reaction reported by Lundquist and co-workers[22] which may occur due to the copper, nickel, or zinc ions released by Novocaine or Xylocaine if they are left very long in contact with the metal. Therefore, the anesthetic solution should not be placed in a metal container or in the syringes until ready to be used.

Akinesia of orbicularis

As previously mentioned, van Lint, in 1914, was the first to advocate blocking the facial nerve to produce paralysis of the orbicularis muscle. Although there have been modifications and different sites suggested for the injections to block the facial nerve, the van Lint method is still popular. Many do a so-called van Lint which is quite different from van Lint's description (fig. 5) which is as follows:

> Introduce the needle one centimeter back of the intersection of a horizontal line extending from the lowest part of the inferior margin of the orbit and a vertical line from the most temporal part of the lateral margin of the orbit. The needle is introduced as far as the bone and directed inward and slightly downward into the deep tissues just below the orbital margin. The injection is given as the needle is withdrawn. Through the same opening in the skin, the needle is again inserted as far as the bone and directed upward and inward near the orbital margin close to the bone.

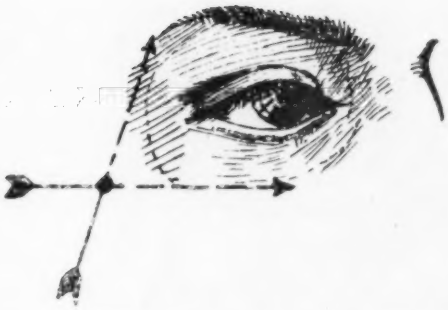


Fig. 5 (Atkinson). The van Lint injection to produce temporary paralysis of the orbicularis muscle. (from van Lint.)

Van Lint in his original report pointed out that an injection may be made around the trunk of the nerve but that this would cause facial paralysis which is undesirable. Villard,[23] in 1919, added to the van Lint injection by making three more injections fanning out from a point about two cm. temporally from the external canthus and directed toward the parotid region. These additional injections seem unnecessary if van Lint's directions are followed.

In 1921, Wright[24] reported making injections from the center of the zygoma to the pinna and another from the same point to below the center of the inferior orbital margin. He states that subsequently he read van Lint's and Villard's earlier reports of a similar method of blocking the nerve supply to the orbicularis. Later in 1923, Wright,[25] desiring a more complete facial paralysis for some of the unruly patients encountered in India, advocated blocking the facial nerve near the stylomastoid foramen. Three years later he published his technique[26] and stated that in some instances the facial paralysis lasted as long as three months which influenced adversely its adoption.

Other modifications of blocking the nerve supply to the orbicularis muscle have been advocated but probably the two most commonly used are the van Lint and the more proximal site advocated by O'Brien.[27]

My principle objection to the van Lint injection was that more anesthetic solution is required than for a more proximal injection. The larger injections increase the risk of a toxic reaction and in the early twenties there were still frequent reports of fatalities due to local anesthesia.

When O'Brien, in 1927, advocated injecting the nerve over the site of the condyloid process which only required about two cc. of the anesthetic solution, it seemed much safer and more efficient so I changed and used this method for about 20 years. However, many patients objected to it because of the pain experienced at the time of the injection and for several days after the operation on moving the jaw, although care was observed not to prick the periosteum of the condyloid process. The lower branches of the facial nerve which supply the lips and face were frequently blocked producing facial paralysis which also disturbed patients. Occasionally the nerve was not blocked because, as pointed out by Kline,[28] the course of the nerve frequently varies and may cross the mandible much lower than the condyloid process (fig. 6).

To overcome these objections a different site for the injection[29] was found to be simpler and more effective than either the van Lint or O'Brien.

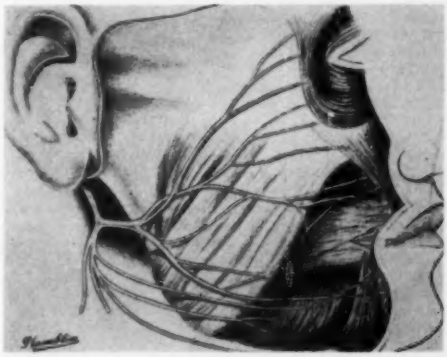


Fig. 6 (Atkinson). Branches of the facial nerve which supply the orbicularis muscle crossing the mandible too low to be blocked by an injection over the condyloid process in front of the tragus. (After Tandler modified by Klein.)

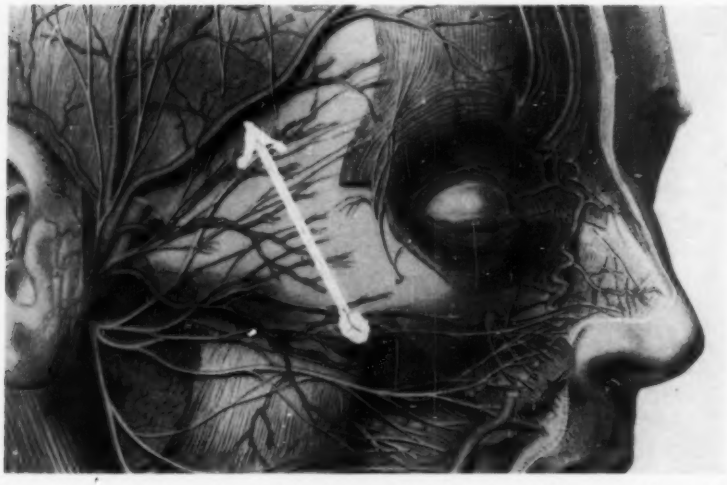


Fig. 7 (Atkinson). Arrow shows site of injection close to the bone which will produce akinesia of the orbicularis muscle regardless of where the nerve crosses the mandible.

Method of injection

This injection is begun at the inferior edge of the zygomatic (fig. 7) bone about in line with the lateral margin of the orbit. The needle is directed upward, close to, and across the zygomatic bone at an angle of about 30 degrees from the vertical. Three or four cc. of the anesthetic solution are injected as the needle advances and firm pressure is exerted over the site of the injection to produce a more rapid and complete block. An important point is that the bony landmarks for the injection at this site can be easily located. With this injection one rarely fails to obtain complete akinesia of the orbicularis. After using it for over six years, no disadvantages have been encountered.

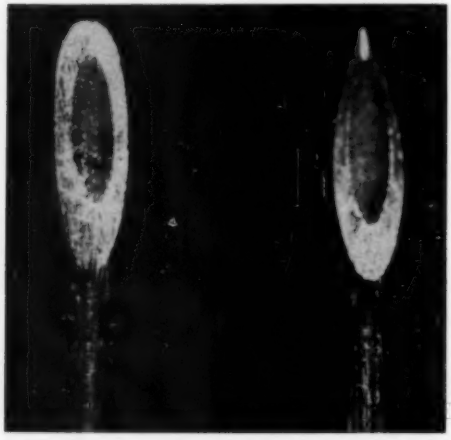


Fig. 8 (Atkinson). Rounded point, 23-gauge, 3.5-cm. needle, and a regular sharp-pointed needle for comparison.

Retrobulbar injection

All are familiar with the value of retrobulbar injections. There are a few points in connection with the injection which, although well known, are often disregarded. As an example, 30 years ago, Duverger[30] called attention to the danger of using a five-cm. needle in making the retrobulbar injection but many surgeons still use a long needle. If a 3.5-cm. needle is used, complete anesthesia and akinesia can be obtained without the danger of piercing the optic nerve or a vessel, or of passing through an orbital fissure or foramen. The use of a 3.5-cm. 22- or 23-gauge needle with rounded point for over 20 years in my practice has proved to be safe and most satisfactory (fig 8). During this time, no orbital hemorrhages or other complications due to the needle have occurred.

The needle with rounded point does not penetrate the tissues as easily as a sharp pointed needle but if the needle is rotated to produce a boring effect it will penetrate the tissues easily.

For years the size of the retrobulbar injection advocated has been 1.0 to 1.5 cc. This is ample to produce anesthesia of the globe but not for akinesia of the rectus muscles. When hyaluronidase is added to the anesthetic solution the size of the injection may be safely increased to 3.0 to 4.0 cc. or more. With pressure the proptosis quickly subsides. The larger injections produce better anesthesia, akinesia, and more marked hypotony.

It has been known for many years that a retrobulbar injection lowers the intraocular pressure. For this reason, Elschnig, over 30 years ago, advocated making the section and doing the extraction immediately after giving the retrobulbar injection before the eye became soft. He considered it desirable to have a firm eye to facilitate tumbling the lens.

After visiting Elschnig in 1929, I adopted many of the excellent measures which he advocated but not the firm eye. Vitreous loss seemed to me more likely to occur if the eye was firm so I not only waited five to 10 minutes after the retrobulbar injection but used rotary massage with pressure over the eye.

The advantages of using pressure following retrobulbar and other anesthetic injections have been known for many years. It is not a new procedure as one might think from the emphasis it has received in the past few years. Török,[31] in 1915, taught me to apply pressure over the site following the injection of an anesthetic solution and Siegrist[32] recommended it as early as 1907 and no doubt others may have before this.

It was also observed[33] that the anterior chamber appeared to be deeper following the retrobulbar injection which indicated a decrease in the vitreous pressure. This strengthened my belief[34] that the lowered vitreous pressure was due in a measure to a decrease of blood within the choroid and ciliary body. The decrease of blood was thought to be the result of constriction of the arteries entering the globe caused by the epinephrine. It was also noted that if the concentration of epinephrine in the anesthetic solution was increased the hypotony increased. Deep rotary massage or pressure over the eyeball produced even greater hypotony and also more complete akinesia of the rectus muscles which in turn decreased the pressure of the muscles on the globe and thus accounted in a measure for the hypotony.

Fig. 9 (Atkinson). Retrobulbar injection given down and temporally. The needle is introduced through an intradermal wheal below the orbital margin temporally and the orbital septum close to the bone. The patient is directed to look upward and nasally so as to move the inferior oblique muscle and the fascia between the lateral and inferior rectus muscles forward and upward, out of the way.

Two points in regard to the use of pressure deserve emphasis:

1. The pressure and massage should be continued until the eye is immobile and soft rather than having a set number of minutes.

2. The pressure should be interrupted frequently to avoid prolonged interference with the retinal circulation.

You may have seen Swan's[35] excellent moving picture showing empty retinal arteries when pressure was made on the globe. Alternating rotary massage of the globe and pressure will produce the desired result with

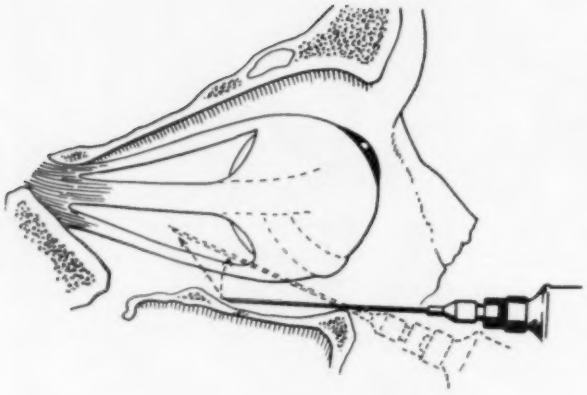


Fig. 10 (Atkinson). The needle is first directed straight back, well away from the eyeball, until the point is beyond the globe. It is then pointed upward toward the apex of the orbit and inserted to a depth of 2.5 to 3.5 cm. and the injection made in the muscle cone. Introducing the needle in this manner avoids tissues that if pierced might bleed. The eye is turned upward and nasally so the inferior oblique muscle and fascia between the lateral and inferior rectus muscles are forward and upward, out of the way.

less danger of affecting the retinal circulation.

When the retrobulbar injection is given down and temporally, good anesthesia and akinesia of the superior rectus muscle is not always obtained.

When the injection is given above and temporally, the angle of approach to the muscle cone is not so good as when given down and temporally. This is more pronounced if the eye is deeply set with a prominent brow. I have obtained better results when the retrobulbar injection is given below and temporally (figs. 9 and 10) and, after a wait of two minutes for the anesthesia to develop, as suggested by Kennedy,[36] a second injection is given above and temporally (fig. 11) at a depth of three cm. near the superior rectus muscle. On withdrawing the needle, when the point is just anterior to the septum, if it is redirected and an injection of 1.0 to 1.5 cc. of the anesthetic solution is made along the superior orbital margin (fig. 12) in the vicinity of the superorbital notch, good anesthesia of the upper lid is obtained. This is done to prevent pain in case a suture is used to close the lid or if the lid is grasped with forceps to open or close the eye following the operation.

Fig. 11 (Atkinson). Injection three cm. back near superior rectus muscle; the lid is held up with a strabismus hook and the patient looks down to facilitate the injection.

If either the lateral or medial rectus muscle is active after the retrobulbar injection, an injection similar to the one near the superior rectus muscle (fig 13) may be given to produce complete akinesia before beginning the operation.

Choice of local or general anesthesia

Let us consider briefly the reasons which influence our choice of local or general anesthesia and some of the advantages and disadvantages of each. Usually the ophthalmologist decides whether local or general anesthesia is to be used and our choice is influenced by several factors: (1) the patient; (2) the type of operation; (3) the experience and skill of the person who is to administer the anesthetic; (4) our early training.

Most eye operations on adults can be done safely and painlessly with local anesthesia which is the preference, when practical, of about 90 percent of the ophthalmologists in the United States. The advantages of local anesthesia will be briefly outlined later.

It should not be forgotten that, if patients are to have a general anesthetic, it is not only our responsibility to select a good anesthetist but to confer with him in regard to the method best suited for the patient and operation that is contemplated. This is often not practical or possible in large hospitals where there are relatively few eye operations that require general anesthesia compared to those done in general surgery. Often the anesthesia for eye surgery is not considered of sufficient importance to demand the services of the more experienced anesthetist so less experienced members of the anesthetic staff may be delegated to administer the anesthesia for the eye department.

Some ophthalmologists operate in small general hospitals in which there may not be an experienced anesthetist. Here the anesthetic may be given by a general practitioner whose limitations should be recognized.

Fig. 12 (Atkinson). Injection along orbital margin to supraorbital notch.

Fig. 13 (Atkinson). Injection three cm. back near lateral rectus muscle. The muscle is grasped with forceps and the eye rotated nasally to facilitate the injection. The same procedure may be used on the medial rectus when indicated.

The usual indications for general anesthesia are: (1) babies and young children; (2) extensive operations on adults—(a) orbital tumors, (b) exenteration, (c) some plastic operations particularly when there is extensive scarring; (3) patients who object to local anesthesia; (4) some mental patients.

There are instances in which general anesthesia is definitely indicated and desirable for ophthalmic surgery but it seems unwise to use it routinely for intraocular surgery as is advocated by a few ophthalmologists. We should keep in mind the hazards and disadvantages of general anesthesia for eye surgery when choosing the type of anesthesia to be used.

Gartner and Billet[87] have conservatively

estimated that 45 deaths with general anesthesia occur during eye operations by certified ophthalmologists each year in the United States.

In a survey of 10 university hospitals, Beecher and Todd[38] found the anesthetic death rate disproportionately high in the first decade of life. Other reports indicate that it is also high in patients over 65 years of age.

For the average ophthalmologist the most frequent major operation is cataract extraction and often he does more of these than all other major eye operations combined. A large proportion of these patients are elderly and not good candidates for general anesthesia. Papper[39] in his excellent paper entitled, "Anesthesia in the aged," states that some older patients are so brittle that "even a gentle breeze of anesthetic gas or vapor seems to be a dangerous stress." He also comments that for these elderly patients local anesthesia offers maximum safety.

An enthusiastic report by Moore[40] on the use of general anesthesia for cataract surgery states that it is the choice of three London hospitals. The results reported do not seem to warrant the enthusiasm that he expresses. He reported iris prolapse in five cases, vitreous loss in two, and two eyes lost in 100 cases done with general anesthesia. An addendum stated that in the next 72 extractions there was one death. Moore emphasizes the importance of using more corneoscleral sutures when operating with general anesthesia because of the postoperative coughing and vomiting. This admonition seems wise.

Other reports of results obtained in cataract surgery when done routinely with general anesthesia do not compare favorably with the results obtained when local anesthesia is used.

The second most frequent operation done by the average ophthalmologist is for strabismus. Usually this is for children under the age of 10 years, in whom the mortality rate reported is particularly high. Although rare, we should keep in mind the oculocardiac reflex and request the anesthetist to watch the blood pressure and pulse continuously, preferably with a monitor. If the pressure and pulse drops markedly with traction on the muscle, the traction should be discontinued and the anesthetist should be ready to inject atropine sulfate (0.1 to 0.2 mg.) intravenously which has been said to counteract the reaction.[41] However, with marked hypotension and sluggish circulation the atropine may not reach its goal. Inflation of the lungs with 100-percent oxygen has been found more effective by Chang, et al.[42]

For intraocular surgery pentothal sodium combined with a local or general anesthetic is used quite extensively. It should be remembered that while pentothal sodium is a potent hypnotic it has a minimum analgesic effect so in a large enough dose to produce anesthesia it is distinctly dangerous because there is such a small margin of safety between this stage and respiratory arrest. For this reason anesthetists advocate the use of a local or general anesthetic with pentothal sodium.

Cullen[43] emphasizes the danger of laryngeal spasm when using pentothal sodium and the importance of controlling the airway during, and for some time after, the operation. During the administration of pentothal sodium in many hospitals intubation is required. While this is an excellent way to maintain an airway and to administer anesthesia it is not without risk. The following complications have been reported following intubation: (1) tracheal edema, (2) laryngeal spasm, (3) pneumonia, (4) lung abscess, (5) atelectasis, (6) cardiac arrest, (7) coughing during recovery, and (8) sore throat and hoarse voice for several days following the operation.

These hazards and discomforts should be considered when choosing the type of anesthesia if we are to avoid complications and have the operation as safe and pleasant as possible.

It is generally conceded that vomiting is much more frequent following general than local anesthesia. It should be remembered

that following a severe eye or other injury all digestion stops for six or more hours. The danger of general anesthesia on a full stomach is well known and should be taken into consideration when planning the anesthetic for repair of an injury. Few adults and fewer children have empty stomachs in the United States.

It is customary and the usual procedure to try to repair eye injuries as soon as possible but, if we thoughtfully review our eye injuries, most will agree that immediate repair has rarely been necessary or advisable. If a dressing is applied and the patients kept quiet with some sedation until they are in proper condition for local or general anesthesia, whichever is deemed advisable, fewer complications will occur and better results will be obtained.

Bonica[44] in his excellent paper praising regional anesthesia states that it causes the least possible disturbance to bodily functions.

Some of the advantages of local anesthesia over general anesthesia are:

1. Earlier ambulation and oral feeding are safer.
2. Less nausea and vomiting occur.
3. There is a lower incidence of pulmonary and embolic complications.
4. There is less bleeding.
5. The secretions are controlled better.
6. The electrolyte balance, blood chemistry, and bodily functions are not upset.
7. There is less danger of aspiration pneumonia, respiratory depression or failure.
8. The risk of explosion is eliminated.
9. The patient requires less nursing care following operation which is an important consideration with the present shortage of nurses.

Summary

In the brief review of the development of ophthalmic anesthesia it is notable how frequently there is a lapse of many years before an important observation, or discovery is recognized or adopted by the medical profession.

It was over 40 years after the anesthetic property of nitrous oxide was suggested by Davy before Wells used it to produce anesthesia for the extraction of teeth.

It was over 20 years after the anesthetic effect of cocaine was reported by Neiman before Koller reported its use as an anesthetic for eye surgery.

The anesthetic procedure of nerve block was reported 30 years before an ophthalmologist, van Lint, thought of using it to block the facial nerve. Then 40 years passed before a single injection across the zygomatic bone was found to be easier, safe, and an efficient way to produce akinesia of the orbicularis muscle. I hope you won't wait 30 to 40 years before adopting it just to keep up the old tradition.

Over 30 years elapsed after Knapp reported a retrobulbar injection before it was used to any extent.

For over 20 years a 3.5 cm. needle with rounded point for retrobulbar injections has been advocated. With it orbital hemorrhages are reduced practically to zero, yet it is not generally accepted.

The use of hyaluronidase in the anesthetic solution causes greater diffusion which allows one to give much larger retrobulbar injections safely. The larger injections produce more complete akinesia and marked hypotony, yet many ophthalmologists still limit the size of the retrobulbar injection to 1.0 or 1.5 cc.

For over 50 years pressure over the site of an anesthetic injection has been recommended but comparatively few eye surgeons have practiced it until recently.

Reports in the literature indicate that there are more complications when intraocular surgery is done with general anesthesia than with local anesthesia, yet some ophthalmologists still employ general anesthesia routinely.

In conclusion I want to thank you again for giving me this opportunity to pay tribute

to the memory of Sandy Gifford, a broad-minded ophthalmologist who was always on the alert to recognize advances in ophthalmology. I sincerely appreciate the great honor that you have conferred upon me. I also want to thank you for your kind attention and your warm hospitality which I am enjoying tremendously.

161 Clinton Street.

References

1. Moodie, R. L.: Studies in paleopathology. (Frontispiece.) Ann. M. Hist., **5**:374, 1923.
2. Severino, M. A., and Bartholinus, T.: In Robinson, V.: Victory over Pain. New York, Henry Schuman, 1946, pp. 40 and 298.
3. Robinson, V.: Ibid., p. 79.
4. Davy, H.: Researches, chemical and Philosophical: Chiefly concerning nitrous oxide, or dephlogisticated nitrous air, and its respiration. London, 1800.
5. Garrison, F. H.: An Introduction to the History of Medicine. Philadelphia, Saunders, 1922, ed. 3, p. 540.
6. Darwin, F.: Eugenics Review, 1914.
7. Brown, T.: Alexander Wood: A sketch of his life and work. Macniven and Wallace, Edinburg, 1886. Eulenburg, Albert: Die hypodermatischen Injection der Arzneimittel. Hypodermatische Methode, Berlin, Hirschwald, 1867, ed. 2, Sect. 4, p. 9.
8. Gaedcke: Arch. d. Pharm., **121**:141, 1855.
9. Neiman: Inaugural dissertation, Göttinger, 1860.
10. Scherzer: Ueber die Peruanische Coca. Stuttgart, 1860.
11. von Anrep: Arch. f. d. ges. Physiol., **21**:38, 1880.
12. Coupard and Bordereau: Seances & Mém. Soc. biol., Serie 8, 1880, p. 1.
13. Koller, C.: Ber. über d. ophth. Gesellsch., Heidelberg, **16**:60, 1884.
14. Knapp, H.: Arch. Ophth., **13**:402, 1884.
15. Hall and Halsted: New York M. J., Dec. 6, 1884, p. 643.
16. van Lint, M.: Ann. ocul., **151**:420-424, 1914; Policlin. Brux., **23**:177-180, 1914.
17. Einhorn, A.: München. med. Wchnschr., **46**:218, 1899.
18. Takamine: Therap. Gaz., **17**:221, 1901.
19. Atkinson, W. S.: Arch. Ophth., **16**:501, 1936; Am. J. Ophth., **31**:1614, 1948.
20. Breinin, G. M., Prof. Ophth. N.Y.U., New York.
21. Atkinson, W. S.: Arch. Ophth., **42**:631, 1949.
22. Lundquist, B., Lofgren, N., Persson, H., and Sjøgren, B.: Acta. Chir. Scandinav., **97**:239-258, 1948.
23. Villard, H.: Bull. Soc. franç. ophtal., 1919; An. ocul., 1919, pp. 352-364.
24. Wright, R. E.: Am. J. Ophth., **4**:445-446, 1921.
25. ———: Arch. Ophth., **52**:166-167, 1923.
26. ———: Arch. Ophth., **55**:555-559, 1926.
27. O'Brien, C. S.: Tr. Sect. Ophth., A.M.A., 1927, p. 250.
28. Kline, M.: Brit. J. Ophth., **30**:668-675, 1946.
29. Atkinson, W. S.: Am. J. Ophth., **36**:1255-1258, 1953; Later modification, Tr. Am. Acad. Ophth., 1956, p. 378.
30. Duverger, C.: L'Anesthésie Locale en Ophtal., Paris, Masson & Cie, 1920.
31. Török, E.: Personal communication.
32. Seigrist, A.: Klin. Monatsbl. f. Augenh., **45**:106, 1907.
33. Atkinson, W. S.: Arch. Ophth., **16**:501, 1936.
34. ———: Tr. Am. Ophth. Soc., **32**:428, 1934.
35. Swan, K. C., and Bailey, P., Jr.: Cinematography of human retinal vessels. Univ. Oregon, Portland, Oregon, 1959.
36. Kennedy, J. A.: Personal communication.
37. Gartner, S., and Billet, E.: Am. J. Ophth., **45**:847-849, 1958.
38. Beecher, H. K., and Todd, D. D.: A Study of Deaths Associated with Anesthesia and Surgery. Springfield, Ill., Thomas, 1954.
39. Papper, E. M.: Bulletin, N.Y. Acad. Med., **32**:635-642, 1956.
40. Moore, J. G.: Brit. J. Ophth., **42**:723-725, 1958.
41. Clinical Anesthesia Conference: N.Y. State J. Med., Sept. 15, 1958, pp. 2992-2993.
42. Chang, J., Macartney, H. H., and Graves, H. B.: Can. Anaes. Soc. J., **4**:191, 1957.
43. Cullen, S. C.: Anesthesia in General Practice. Chicago, Year Book, 1949 ed. 2, p. 84.
44. Bonica, J. A.: J.A.M.A., **168**:734-742 (Oct.) 1958.

MISTAKEN DIAGNOSES IN SOME CASES OF MENINGIOMA*

Clinics in Perimetry No. 5

C. Wilbur Rucker, M.D., and Thomas P. Kearns, M.D.
Rochester, Minnesota

Meningiomas that originate near the intracranial portion of the optic nerves give rise to a variety of defects in the fields of vision. When the defect exhibits a midline step, the location is usually evident. It is the central scotoma that worries the neuro-ophthalmologist, especially when, as is too often true, there are no other findings on neurologic examination, and roentgenograms of the skull fail to show changes in bone. The case histories presented in this paper illustrate the difficulties occasionally encountered in arriving at a correct diagnosis and the factors responsible for the confusion.

Meningiomas characteristically grow slowly and give rise to symptoms that progress gradually. The episodic course pursued by some of them may lead the examiner astray, as in the following case:

Case 1

A man, aged 29 years, registered on July 30, 1959, complaining of loss of vision in the right eye. He stated that late in 1957 he had had loss of vision in that eye for three weeks with spontaneous recovery, and that an ophthalmologist told him at the time that the nervehead was elevated. Early in 1959 he had had loss of vision in the left eye for one week, again with spontaneous recovery. In April, 1959, he had diminution of vision in the right eye with some improvement after a few days but without complete recovery. Since May he had had pain around the region of the right eye which was increasing at the time of admission, and he also had had some bulging forward of the right eye. He had consulted several neurologists and ophthalmologists in his home community without receiving a diagnosis. Treatment had consisted only of eyedrops.

Vision of the right eye on admission was 20/60, that of the left 20/20. The right optic nervehead was elevated four diopters by chronic edema; the left nervehead was flat and pale. Exophthalmometer readings on the Hertel instrument were 16.5 mm. for the right eye and 13.5 mm. for the left. As indicated in Figure 1, the field of the right eye was contracted nasally and the field of the left eye was full. A roentgenogram of the head showed no changes in the bone. The examiner noted that the patient's history of recurrent episodes of visual loss suggested a diagnosis of optic neuritis but that the findings were those of basal frontal tumor.

A right carotid angiogram showed that the right anterior cerebral artery was elevated by a suprasellar mass. A few days later the neurosurgeon carried out a right transfrontal craniotomy and encountered a large meningioma which had taken its origin on the tuberculum sellae and overlay the visual apparatus. In spite of the left optic nerve being compressed by the tumor and the right optic nerve being completely surrounded by it, he was able to remove the tumor completely. He noted that the proptosis must have been on the basis of vascular obstruction because the tumor had not extended into the orbit.

When the patient returned for observation on October 6, 1959, it was found that the field of the left eye was nearly normal, but that the right eye was essentially blind.

In the above-described case, absence of proliferation or destruction of bone on roentgenography left the examiner without visible evidence of meningioma. The episodic course, although not uncommon in meningioma, is certainly not characteristic.

Meningiomas expand rapidly during pregnancy, apparently in part by acceleration of growth and in part by increase in vascularity. Consequently, pregnancy intensifies the symptoms of these tumors, as in the following case:

Case 2

A woman, aged 41 years, registered on November 13, 1959, complaining of severe loss of vision in both eyes. On September 20th she had noted the onset of rapid loss of vision in the right eye followed two days later by loss in the left. Vision had declined rapidly since then. A constant ache was present above and behind both eyes and extended into the occipital region. She had consulted several ophthalmologists and neurologists in her home community but her physicians could not find the cause of her trouble. Their tentative diagnosis had been retrobulbar neuritis, and treatment had consisted of steroids. The patient had been using a hair spray once a week for the past year and she was pregnant five and one-half months.

* From the Section of Ophthalmology, Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

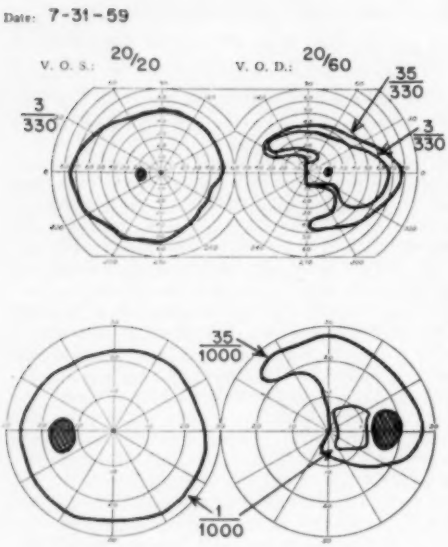


Fig. 1 (Rucker and Kearns). *Case 1.* Contraction of the field of the right eye.

On admission the vision of the right eye was 2/200; vision of the left eye was reduced to light perception. The visual fields, shown in Figure 2, were restricted to small isles in the field of the right eye. Ophthalmoscopic examination disclosed slight pallor of the right optic nervehead and moderate pallor of the left. The ophthalmologist wondered if the lesion could be a meningioma at the tuberculum sellae with visual loss accelerated by the rapid growth of the meningioma during pregnancy.

Neurologic examination yielded no abnormal findings, and a roentgenogram of the head showed no evidence of disease. A tentative diagnosis was made of a lesion at the optic chiasm, type undetermined, and it was recommended by the consulting neurosurgeon that angiography be performed. This demonstrated a mass lesion in the midline in the region of the tuberculum sellae which elevated both anterior cerebral arteries. On November 21st the neurosurgeon performed a right transfrontal craniotomy and found a meningioma which had arisen from the left anterior clinoid and had grown to the midline. He was able to remove the entire tumor. The visual fields charted at the tangent screen on November 30, 1959, were nearly normal (fig. 3).

The scotomas of bilateral involvement of the optic nerves by tumor may simulate those of toxic amblyopia. A known exposure to poison may readily mislead the examiner, as in the following case.

CASE 3

A 30-year-old draftsman registered on September 25, 1958, having been referred by his local oculist with the tentative diagnosis of retrobulbar neuritis in the right eye. Four months previously he had noted gradual onset of loss of vision in the right eye. He had been working hard and his wife had been ill and he thought that those factors might have been responsible. Treatment had consisted of intramuscular injections of vitamin B_{12}.

On examination the fundi appeared normal. The perimetric fields shown in Figure 4 demonstrated a large central scotoma in the field of the right eye which broke through inferonasally. The field of the left eye was depressed inferiorly. One of us (C.W.R.) recommended a general and neurologic examination and noted that the patient lived in an old house where the water pipes were made of lead. He obtained from the patient information that during the previous spring he had used several toxic sprays on fruit trees. General physical examination yielded no abnormal findings. The X-ray appearance of the head and the results of a flocculation test for syphilis were normal. Eleven percent of the cells in a blood smear were eosinophils. The patient was dismissed on September 30th with the diagnosis of bilateral involvement of the optic nerves which could have been on the basis of toxins used in spraying fruit trees. Upon dismissal he asked if another consultation might be advisable and we urged that he obtain it.

A letter from the referring physician received on January 5, 1959, stated that the patient had seen a prominent ophthalmologist in Chicago on several occasions and, because of the progression of his

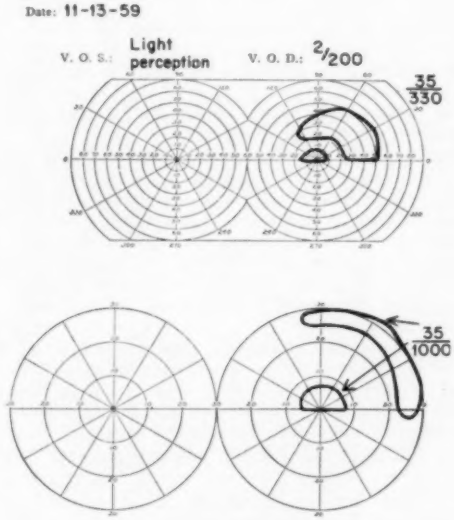


Fig. 2 (Rucker and Kearns). *Case 2.* Isles of vision.

visual disturbance, had been referred to a neurosurgeon. The latter found that there was loss of his sense of smell on the left side and made a carotid arteriogram, which disclosed an upward displacement of the anterior cerebral artery that was strongly suggestive of a midline tumor. He noted also a faint calcific shadow in the same region. He performed a transfrontal craniotomy on December 18th and removed a large midline meningioma weighing 30 gm. which had arisen from the tuberculum sellae and had displaced both optic nerves laterally and the chiasm posteriorly. He stated that the patient had done quite well in his postoperative course, but did not enclose charts of the visual fields.

Bilateral scotomas in a patient who was a chronic alcoholic led one of us (C.W.R.) to a wrong diagnosis on still another occasion.

CASE 4

A woman, aged 50 years, was admitted on January 11, 1956, with the complaint of loss of vision which had begun in May, 1955, and had been gradually progressing. By October, 1955, her vision had become worse and her physician could find no explanation for it. Vision continued to diminish to the point where she could no longer recognize people. She lived alone and ate most of her meals out. Her husband, who had been a tavern keeper, had died in 1950 and the patient had then taken over management of the tavern. She lived in the same building and had been drinking heavily since then. Her admitted intake of alcohol was several cocktails a day, and she smoked one pack of cigarettes daily. In May, 1955, when her vision began to fail, she sold the tavern and since then had been drinking on only one or two days a week, when she had seven to nine highballs. Treatment had consisted of vitamin B_{12} and nicotinic acid.

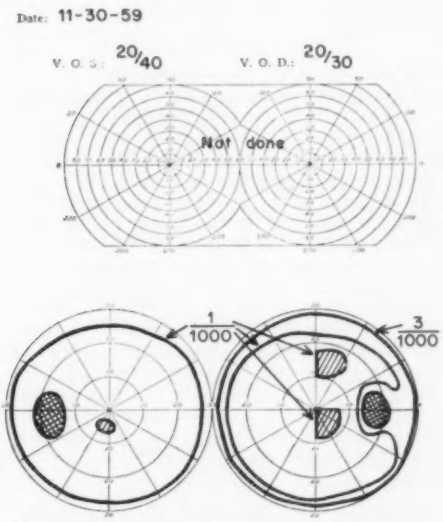


Fig. 3 (Rucker and Kearns). *Case 2.* Postoperative visual fields.

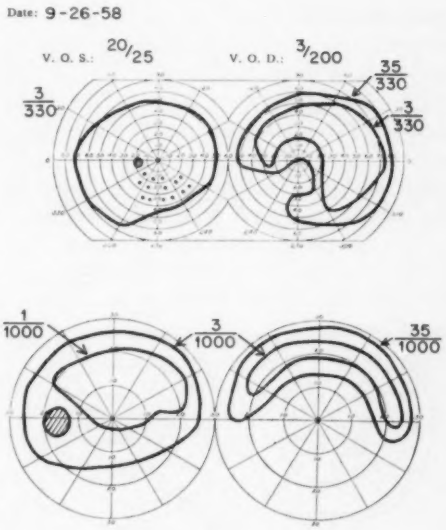


Fig. 4 (Rucker and Kearns). *Case 3.* Inferior altitudinal contraction.

On examination her visual acuity was 3/200 in each eye. Examination of the visual fields demonstrated the presence of cecocentral scotomas as shown in Figure 5. The optic nerveheads were slightly pale. The results of neurologic examination were negative except for absence of the sense of smell which the patient said she had had for about six years. A roentgenogram of the head showed no evidence of disease. The tentative diagnosis was toxic amblyopia due to avitaminosis from excessive intake of alcohol; this was made with some reluctancy, for we had never before seen such large scotomas in this disorder. The patient was advised to give up alcohol but she was reluctant to agree to do so. She was given a prescription for vitamin-B complex and was dismissed on January 16, 1956.

A letter in June, 1956, from one of her daughters stated that, although she had been told on dismissal that her vision would improve, it had not improved but had become worse during the previous five months.

Another daughter wrote in November, 1957, that the patient had taken the vitamin pills faithfully for a year and a half but that they had not been of any benefit and that at the time of this letter the patient was completely blind. She stated that her mother refused to do anything about her vision and would not consult other physicians. In Febru-

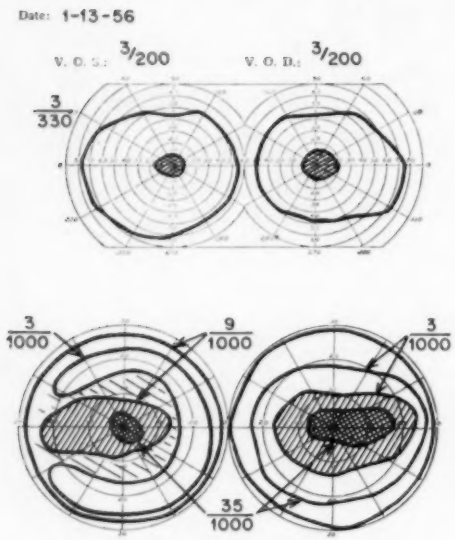


Fig. 5 (Rucker and Kearns). *Case 4.* Cecocentral scotomas.

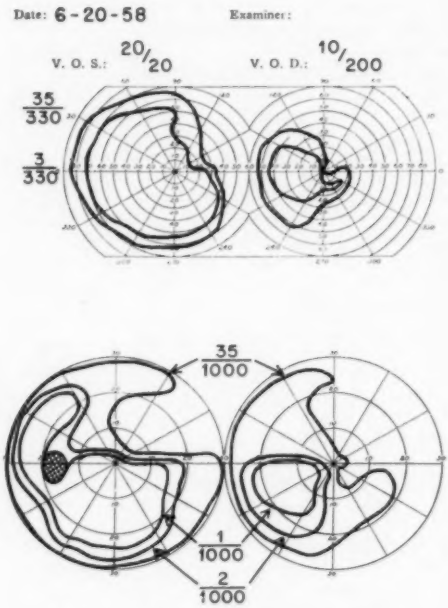


Fig. 6 (Rucker and Kearns). *Case 5.* Irregular contraction.

ary, 1959, a physician in the patient's home town wrote that he had performed a vaginal repair for her under general anesthesia and that she never recovered from the anesthesia, but died that evening. Examination of the head at necropsy disclosed the presence of a meningioma six cm. in diameter which had arisen from the floor of the calvarium anterior to the sphenoid sinus where it was attached to the underlying meninges.

The presence of hyaline masses on the optic discs in a case of slowly progressive visual loss masked the real culprit in the following case.

CASE 5.

A woman, aged 43 years, registered on June 19, 1958, with the complaint of failing vision since September, 1956. At that time a complete physical examination and X-ray examination of the head had disclosed no evidence of disease and her oculist had prescribed nicotinic acid and some other expensive white tablets. In March, 1957, when the visual loss had progressed, further examinations were conducted, again with negative findings. Vitamins, desiccated thyroid and neostigmine were prescribed. The patient stated that at first only her side vision was affected and that only recently had central vision become involved.

Visual acuity of the right eye was recorded as 10/200, that of the left eye 20/20. Ophthalmoscopic examination disclosed moderate pallor of both optic discs and the presence of very large, numerous hyaline masses in the deeper portions of the discs. The visual fields were contracted, with involvement of the central area of the right (fig. 6). Some of the loss was in the nature of arcuate defects. One of our associates saw the patient and concluded that the visual loss was probably on the basis of the hyaline masses. On the chance that the patient might have hyaline masses and in addition some other disease of the optic nerve, he ordered X-ray examination of the head, complete neurologic examination and the usual laboratory tests. The results of all of these were within the range of normal. Before dismissing her on June 25th, he asked that one of us (C.W.R.) see her in consultation. The latter examiner agreed that the hyaline masses appeared to be responsible for the visual loss and permitted the patient to be dismissed.

On August 14, 1958, a letter was received from a neurosurgeon in Cincinnati who wrote that arteriograms made two days previously did not show any abnormality. On the following day he had explored the region of the right optic nerve and had found behind that nerve a meningioma that had extended over to the left side as well. Postoperatively the patient was blind in the right eye, but vision in the left appeared to have improved. He did not send copies of the visual fields.

On review of this situation, it appeared that we should have taken more seriously the possibility that some other cause for the

loss of the vision might be a factor in addition to the hyaline masses. After receipt of the neurosurgeon's letter we reviewed all our cases in which hyaline masses on the optic nerveheads had produced defects in the visual fields and found that not a single patient had reduced central acuity. Had we been aware of that observation previously, the loss of central vision in this patient would have forced us to search more diligently for some other disease, even to the extent of advising direct exploration.

Comment

These cases illustrate how difficult may be the diagnosis of meningioma in the region of the optic nerves. In general, meningiomas grow slowly and their symptoms progress steadily. The exceptions, such as those that have an episodic course or those whose symptoms are intensified by pregnancy, may plague the ophthalmologist. They simulate retrobulbar neuritis often enough to worry him every time he is forced to venture such a diagnosis. In about 85 percent of cases, a meningioma in the region of the optic nerves and chiasm produces changes that are visible on roentgenography. When these changes are lacking, the ophthalmologist may easily arrive at a mistaken diagnosis.

Mayo Clinic.

UVEITIS*

III. Peripheral uveitis: Pathogenesis, etiology and treatment

R. J. Brockhurst, M.D., C. L. Schepens, M.D., and I. D. Okamura, M.D.
Boston, Massachusetts

Previous reports[1,2] have described a form of granulomatous uveitis in which the earliest pathologic changes occur either in the extreme fundus periphery or the angle of the anterior chamber. It has been observed that granulomatous type exudates may occur in these locations in the absence of similar changes elsewhere in the eye. The importance of gonioscopy and stereoscopic indirect ophthalmoscopy with scleral indentation in discovering these inflammatory changes has been stressed. Otherwise, such cases may be erroneously diagnosed either as nongranulomatous uveitis or as some other disease. In addition, the many and varied complications of peripheral uveitis have been described, and the differential diagnosis has been discussed. Since macular degeneration, choroidal detachment, secondary retinal detachment, vitreous opacities and degeneration, vitreous hemorrhage, vascular occlusion, optic atrophy, cataract, and glaucoma may occur as a result of peripheral uveitis, it is very important to recognize this condition. Unfortunately, in some instances the secondary complications are considered as primary diagnoses, the actual uveitic process being unrecognized due to failure to perform gonioscopy and an examination of the extreme fundus periphery.

In this paper we wish to discuss the pathogenesis, etiology, and treatment of peripheral uveitis based upon observation of 100 patients.

Pathogenesis

As no histologic studies of the early stages of peripheral uveitis are available, the pathogenesis of this clinical picture is not definitely established. However, our clinical examinations seem to indicate that the process may arise in three anatomic areas:

First, the inflammatory focus may lie in

* From the Retina Foundation, Department of Ophthalmology, Massachusetts Eye and Ear Infirmary. (Paper No. 92, Retina Foundation.) This work was supported by Grant No. B633 of the Institute of Neurological Diseases and Blindness, National Institutes of Health, Department of Health, Education and Welfare, Bethesda, Maryland.

the ciliary body itself, be chronic, and result in exudative material and cells being cast into the aqueous humor of the posterior chamber. Exudates may then be deposited in two locations, namely, the trabeculae of the anterior chamber angle, forming trabecular precipitates and the pars plana ciliaris and ora serrata region, forming gelatinous exudates. The gelatinous exudates which are observed clinically have not been studied pathologically. However, their appearance suggests a granulomatous exudate on the retina similar to exudates found by Zimmerman and Silverstein in experimental uveitis in rabbits.[3] These authors injected egg albumin into the rabbit vitreous where it remained as a depot, and caused agglutinated masses of mononuclear cells on the retina projecting into the vitreous cavity (fig. 8 on page 454 of Zimmerman and Silverstein's article).

If the process does not subside, one may subsequently observe that the trabecular precipitates cause anterior synechias which sometimes result in glaucoma. Other sequelae are cyclitic membrane formation from the exudative material on the pars plana; preretinal organization in the fundus periphery, resulting in traction on the retina with subsequent retinal detachment; and complicated cataract.

The second area where the inflammation may begin is the peripheral choroid and pars plana of the ciliary body under the region of attachment of the vitreous base. In this location the exudative material tends to remain under the vitreous base, explaining the paucity of symptoms at this stage. After many months the exudates may enter the posterior chamber aqueous and lead to trabecular precipitates as with the first type. In addition, they may enter the vitreous giving rise to opacities which may be noticed by the patient. Later, secondary changes such as macular edema and degeneration may reduce central vision, and complicated cataracts may develop. It is felt that this form of peripheral uveitis may also be responsible for those cases which develop anterior choroidal detachment and subsequent secondary retinal detachment.

Finally, the initial inflammatory change may occur as a peripheral perivasculitis and retinitis. Tiny exudates appear on the retina adjacent to the small vessels which show sheathing. These exudates may enter the vitreous readily, and for this reason the patient is likely to notice vitreous opacities earlier than with the other forms. If this type of peripheral uveitis continues, there may be progressive obliteration of the retinal vessels with optic atrophy and profound loss of vision. In some cases the perivasculitis leads to localized obliteration of the vessels, followed by neovascularization. The new-formed vessels may proliferate into the vitreous cavity and give rise to vitreous hemorrhages. If the process is less severe, chronic, cystic and degenerative changes may occur in the retina with subsequent retinal break formation and retinal detachment.

Pathologic examination has been performed on three eyes which showed peripheral uveitis early in the course of the disease. In one patient the first changes consisted of perivasculitis in the retina, especially the veins, associated with exudative material on the peripheral retina and in the vitreous cavity. Over the course of three years there was a progressive obliteration of the retinal vessels which extended posteriorly from the periphery, subsequent optic atrophy, severe vitreous hemorrhage, and finally an acute anterior uveitis with pain. Pathologic study showed a fibrous type of iritis, many peripheral anterior synechias, and detachment of the retina. The retinal vessels were noteworthy in that the walls were thickened and perivascular cuffing caused by accumulation of lymphocytes and plasma cells was prominent (fig. 1).

In a second patient, a boy four years of age, massive gelatinous exudates were found in the extreme periphery associated with an inferior cyclitic membrane. Over the course of one year the cyclitic membrane advanced to obscure almost the entire posterior lens surface. Total retinal detachment occurred

Fig. 1 (Brockhurst, Schepens and Okamura). Section of detached retina, showing thickened walls of retinal vessels and perivascular cuffing.

as a consequence of the organizing cyclitic membrane. Pathologic examination revealed a cyclitic membrane with totally detached and organized retina behind the lens (fig. 2). Focal areas of choroiditis containing lymphocytes, plasma cells and eosinophiles were seen in the peripheral choroid (fig. 3).

The third patient was a boy, aged seven years, who initially showed massive gelatinous exudation in the extreme fundus periphery involving all but the superior nasal quadrant. In the course of three years a dense vascularized membrane formed behind the lens beginning inferiorly in the vicinity of the original massive exudate. The retina then became totally detached, no retinal breaks ever being visualized. Gradually a complicated type of cataract formed, and the patient was not seen again for two more years. Five years after the initial examination, he returned with acute glaucoma, the angle being closed and the lens showing a swollen cataract. Pathologically changes similar to those of the second patient were found, cyclitic membrane with totally detached and organized retina.

Etiology

Etiologic investigation included careful ocular and general histories, medical evaluation, and laboratory investigation, such as blood Hinton test, complete blood count, urinalysis, chest X-ray films, old tuberculin skin test, Toxoplasma dye test, or toxoplas-

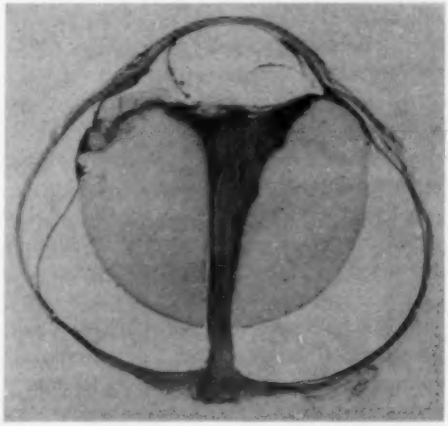


Fig. 2 (Brockhurst, Schepens and Okamura). Section of eye, showing cyclitic membrane which includes the totally detached and organized retina.

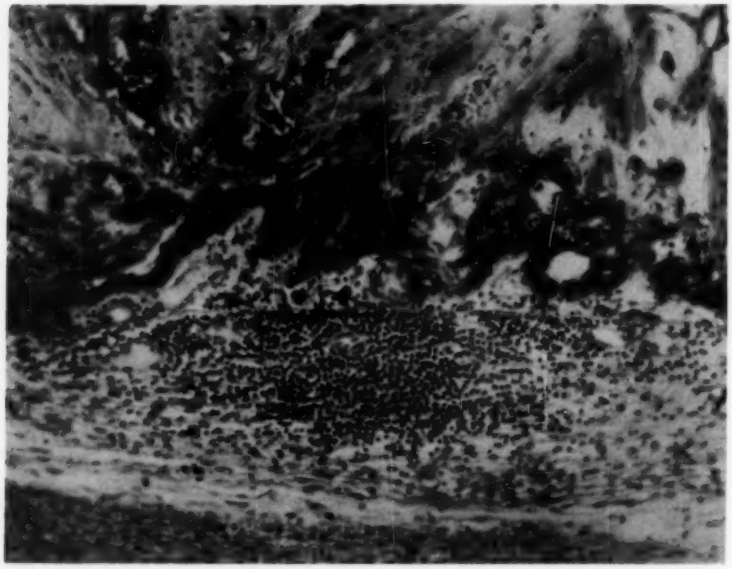


Fig. 3 (Brockhurst, Schepens and Okamura). Focal area of choroiditis located in the peripheral choroid near the ora serrata.

min skin test, nose and throat cultures, brucella agglutination and antistreptolysin titer determination. In addition, lumbar puncture, with cell count and protein determinations of spinal fluid, skull X-ray films, blood total protein determination, prostatic secretion, cultures, histoplasmin skin testing, and stool examinations for ova and parasites were performed in patients where there was an indication for these studies. Streptococcal skin testing was not performed. The possible role of the streptococcus in uveitis has been investigated by other means, and will be the subject of a subsequent paper.

The results of the etiologic study of 100 patients with peripheral uveitis were compared with similar studies in a group of 110 patients in whom granulomatous uveitis was diagnosed by direct ophthalmoscopy or slit-lamp microscopy (table 1).

It can be seen from this table that presumptive diagnoses in the two groups are essentially the same, with the exception of toxoplasmosis. A presumptive diagnosis of toxoplasmosis was made in 27 percent of 110 patients with other forms of granulomatous uveitis, many of whom had chorioretinitis posterior to the equator. On the other hand, of 100 patients with peripheral uveitis, only eight showed laboratory evidence of toxoplasmosis. In more than half of the patients with peripheral uveitis no information was gained which would indicate a possible etiology. Moreover, the presumptive diagnoses which are given in Table 1 cannot be considered as etiologically accurate. Table 2 shows the results of specific treatment in those patients wherein it was felt that the presumptive diagnosis was a significant finding and also the results of nonspecific therapy. The relatively poor results of specific therapy tend to indicate that these presumptive diagnoses were probably inaccurate, except in the case of syphilis.

Treatment

Since peripheral uveitis usually follows a chronic course with remissions and exacerbations lasting for several months, it is most difficult to evaluate the effects of therapy. In

cases where the process appeared to be healing spontaneously, no treatment has been instituted. Eyes showing active signs of inflammation in the anterior segment with a tendency toward either peripheral anterior synechia or posterior synechia formation were treated with local steroids such as 0.5-percent to 2.5-percent cortisone acetate collyrium. Instillations were made three to eight times a day, depending on the degree of inflammation. In addition, the pupil was kept dilated. When the tendency toward peripheral anterior synechia formation is very marked, it may be dangerous to keep the pupil dilated over a long period of time since this brings the periphery of the iris closer to the trabecular precipitates and encourages iris-exudate adhesions. In such cases, the pupil should be dilated once or twice a week with short-acting mydriatics, such as phenylephrine hydrochloride (10 percent) or cyclopentolate hydrochloride (1.0 percent). If there is evidence of posterior synechia formation, it is essential to break them with mydriatics but the pupil should be allowed to return to its normal size at least twice a week. Between these brief periods of mydriasis, the pupil is left undilated as this decreases the risk of peripheral anterior synechia.

TABLE 1

RESULTS OF ETIOLOGIC SURVEY

	Peripheral Uveitis (100 patients)	Ordinary Granulomatous Uveitis* (110 patients)	
	Number and Percent†	Number of Cases†	Percent
Tuberculosis	14	13	12
Toxoplasmosis	8‡	30‡	27
Streptococcal infection	11	6	5
Syphilis	3	3	3
Nematode	3	0	0
Sarcoidosis	2	1	1
Nasal sinus infection	2	0	0
Dental infection	2	0	0
Rheumatoid arthritis	1	3	3
Sympathetic ophthalmia	1	1	1
Heterochromic cyclitis	1	2	2
Phacoanaphylaxis	0	1	1
Gonorrhea	0	1	1
Amebiasis	0	1	1
Histoplasmosis	0	1	1
Harada-Vogt-Koyanagi	0	1	1
None	61	51	46

* As diagnosed with direct ophthalmoscopy and biomicroscopy. Many cases interpreted as nongranulomatous uveitis by these methods are in reality granulomatous when gonioscopy and stereoscopic indirect ophthalmoscopy of the fundus periphery are performed.[2]

† The totals may exceed the number of cases reported since some patients showed evidence of more than one systemic disorder which might be responsible for the uveitis.

‡ Statistically significant difference ($P < 0.05$).

Patients who showed progression of the peripheral uveitis process with increasing signs of exudation and cicatrization have been given specific therapy when a presumptive diagnosis of systemic granulomatous disease was made. However, the results of such treatment have been disappointing except in the case of syphilis (table 2). If etiology was obscure, or if there was no response to specific therapy, systemic steroid treatment was instituted, and almost half of the patients so treated benefited by this treatment (table 2). Steroids have been most effective in cases which showed an acute exacerbation associated with choroidal and/or retinal detachment.[2]

Prednisone was administered in doses of 30 to 60 mg. per day for one to two weeks, then reduced to 20 to 40 mg. per day until the disease process subsided, usually two to three months. ACTH therapy has been used initially in some acute cases, a daily dose of 40 units being given by intravenous drip in 500 cc. of five-percent dextrose in water over a period of four to eight hours, for three to five days. Following this, systemic steroids were given by mouth as already described. It is not clear whether or not such initial ACTH therapy actually offers any advantage over systemic steroids from the start.

Fever therapy has been used in several patients. In some instances, it appears that it may offer some benefit in patients who are not doing well with systemic steroids. If the patient was on systemic steroids imme-

TABLE 2

RESULTS OF TREATMENT

	Peripheral Uveitis			Ordinary Granulomatous Uveitis		
	Cases Treated	Number Improved	Percent Improved	Cases Treated	Number Improved	Percent Improved
Tuberculosis*	8	2	25	3	2	66
Toxoplasmosis†	6	1	16	12	7	58
Streptococcus‡	5	0	0	1	0	0
Syphilis	2	2	100	2	1	50
Amebiasis	0	0	0	1	0	0
Steroid-local	19	14	74	18	9	50
Steroid-systemic	32	15	47	33	20	61
Fever therapy	7	4	57	7	4	57

* Intramuscular streptomycin (one gm. twice a week), para-amino-salicylic acid (10–12 gm. per day), isoniazid (100 mg. three times a day) for at least three months.

† Pyrimethamine (25 mg. three times a day), sulfadiazine (0.5 gm. four times a day for three weeks; then one-third dosage for five more weeks).

‡ Oral penicillin (200,000 units twice a day for at least three months.)

diately before, the steroids should be continued during the period of fever therapy, since the ingestion of steroids tends to cause adrenal atrophy. Sudden withdrawal of steroids followed by intravenous fever therapy might well precipitate signs of adrenocortical deficiency. Theoretically, the effect of intravenous fever therapy would be better if the adrenal gland were normal, so that it would respond fully to the artificially induced fever. If the patient has been on systemic steroids for any length of time, it will then be necessary to withdraw steroids gradually over a period of several weeks before giving the fever therapy. In many patients this procedure may result in a worsening of the uveitic process during the steroid withdrawal, and, therefore, it should not be done unless the physician is certain that such steroid withdrawal will not adversely affect the eye.

To induce fever, 100 million organisms of typhoid-paratyphoid vaccine are used, the organisms being introduced by intravenous drip in 500 cc. of normal saline solution over a period of two to four hours. The rate of flow of the saline-vaccine mixture should be adjusted to maintain a body temperature of about 102°F. Temperatures should be taken every 15 minutes during the infusion. If the temperature rises above 102°F., the rate of flow is reduced, and vice versa. If the temperature rises above 103°F., the infusion should be stopped, salicylates prescribed, and alcohol sponge baths given to bring down the temperature.

COMMENT

Peripheral uveitis should be classified as granulomatous by virtue of the gelatinous type deposits which occur in the anterior chamber angle and in the fundus periphery, its chronic course, and the organic changes which ensue. Generally, patients who show peripheral uveitis are extremely healthy individuals with no evidence whatsoever of systemic disease. This is in agreement with the findings of other authors in more obvious types of uveitis. For example, Gordon reports that only in 29 of 93 patients, or 31 percent, he was able to find an "etiologic clue."[4] Similarly Schlaegel reported a "probable" diagnosis was made in only 17 percent of his 100 cases although "possible" causes were found in 55 percent of the group.[5] In 40 percent of our patients, laboratory studies have revealed positive findings such as tuberculin or toxoplasmin skin tests, evidence of pulmonary calcification, or signs of old nasal accessory sinus infection by X-ray examination, carious teeth, previous streptococcus infection, and so forth. However, in these patients, specific therapy has been disappointing, and the results were generally

parallel to those obtained in patients who were given no specific therapy. On the whole, the use of steroids has not been followed by dramatic results, even with long-term programs of treatment. Gordon, on the other hand, obtained rather good results from systemic steroid therapy in his 93 patients with chronic uveitis. In his paper he stresses the use of high dosage of steroids, for example, 10 to 12 tablets per day of the common preparations such as a five-mg. prednisolone tablet, over long periods of time. Although generally we did not use dosages which were this great, many of our patients developed Cushingoid signs such as weight gain, moon face, acne, osteoporosis, inhibition of growth (in children); and one patient developed a compression fracture of a vertebra. Therefore, we do feel that our steroid therapy dosage approached a judicious therapeutic level.

Patients with peripheral uveitis have been studied for possible allergic diatheses, and the presence of collagen disorders. To date, no increased incidence of these conditions has been detected. However, since the period of follow-up on these patients ranges from only one to eight years, it is possible that in the future, such signs might appear.

At the present time, we believe it important to call attention to this type of uveitis which shows its first signs in the fundus periphery and the chamber angle. It is our hope that this report will stimulate further investigation of peripheral uveitis.

Summary

The pathogenesis of peripheral uveitis is described as observed in 100 patients with this disease. The inflammatory process may begin in the ciliary body resulting in exudative deposits in the anterior chamber angle and the pars plana ciliaris. A second site of onset is the peripheral choroid near the ora serrata region, under the attachment of the vitreous base. Exudative material may remain trapped in this location for many months without causing symptoms. Finally, the process may begin as a perivasculitis of the peripheral retinal vessels, associated with peripheral retinitis and exudates on the retina. Such exudates enter the vitreous and may be noticed as vitreous opacities by the patient early in the course of the disease. Pathologic studies have been possible in only three patients. In all instances, the disease had been present for several years, and late cicatrizing stages of the disease were present.

Etiologic investigations in 100 patients with peripheral uveitis gave similar results as did those in 110 patients with ordinary types of granulomatous uveitis with the exception of toxoplasmosis. A presumptive diagnosis of toxoplasmosis could be made four times as often in the latter group which included many cases of posterior chorioretinitis.

Specific treatment in those cases wherein a presumptive diagnosis was made was not particularly successful except in the case of syphilis. Mild forms of peripheral uveitis can be managed with local medication such as mydriatics and steroids. About one half of the more severe cases were benefited by systemic steroid therapy.

99 West Cedar Street (14).

Acknowledgments

The histologic specimens were prepared at the Eye Pathology Laboratory, Massachusetts Eye and Ear Infirmary, under the direction of Taylor R. Smith, M.D. The photomicrographs were made by Mr. David Feigenbaum, Eye Pathology Laboratory, Massachusetts Eye and Ear Infirmary.

References

1. Brockhurst, R. J., Schepens, C. L., and Okamura, I. D.: Uveitis: I. Gonioscopy. Am. J. Ophth., **42**:545-554, 1956.

2. ———: Uveitis: II. Peripheral uveitis: Clinical description, complications and differential diagnosis. Am. J. Ophth., **49**:1257 (June) 1960.

3. Zimmerman, L. E., and Silverstein, A. M.: Experimental ocular hypersensitivity. Am. J. Ophth., **48**:457-465 (Nov. Pt. II) 1959.
4. Gordon, D.: The treatment of chronic uveitis. AMA Arch. Ophth., **62**:400-413, 1959.
5. Schlaegel, T. F., Jr.: Granulomatous uveitis: An etiological survey of 100 cases. Tr. Am. Acad. Ophth., **62**:813-825, 1958.

CATARACT EXTRACTION WITH THE MODIFIED SMITH TECHNIQUE*

RICHARD A. ELLIS, M.D.
Philadelphia, Pennsylvania

This paper was originally presented at the October, 1958, joint meeting of the Eye Section of the Philadelphia County Medical Society and the Section on Ophthalmology of the College of Physicians of Philadelphia. The purpose was merely to review some principles of cataract extraction of Col. Henry Smith and describe the modified technique of Sir Henry Holland. Recently, since the use of alpha chymotrypsin, the modified method of cataract extraction described may be employed most satisfactorily in many properly selected cases.

Many ophthalmic surgeons, who use a combination of pressure and traction in removing cataracts, believe that modern intracapsular cataract surgery is based on the principles laid down by Col. Henry Smith. They also contend that, while his procedure is too dangerous to use today, it is still worth knowing. Other surgeons who break the zonule directly may agree with Kirby who argued against the employment of Smith's method, contending that it was too traumatic. The following discussion may at least have some historic value to this latter group. Now that the use of alpha chymotrypsin is increasing, extraction with external manipulation alone may again become more popular.

The various types of incisions and sutures will be omitted. It is assumed that the incision will be 180 degrees in extent.

HISTORICAL REVIEW

Most ophthalmologists agree that modern intracapsular cataract surgery became popularized as a result of the work of Col. Henry Smith who first published his procedure in 1903. In the first method that Smith described, a muscle hook is placed on the flat over the lower part of the cornea, the point being above and the heel below (fig. 1). Then the point is sharply twisted backward. In what he describes as the "hard lens," this maneuver would push the lower edge back and cause its upper edge to come forward, stretching the suspensory ligament above and below. In many cases, especially in older persons, with this simple twist the suspensory ligament would break above and below. The lens is then maneuvered out with the gentlest pressure—the point of the squint hook being directed into the fold of the cornea and thus pushing the lens out and folding the cornea behind it (fig. 1-c and 1-d).

Col. Smith admitted that a major difficulty arises when the suepensory ligament is more firmly attached. This would require more pressure initially for the dislocation for which Col. Smith advocated making pressure with the heel of the hook toward the optic nerve, while the point of the hook is pointed backward. This maneuver increases the hydrostatic pressure of the vitreous which in turn presses the back of the lens and drives the upper edge forward where the suspensory ligament breaks first. At this time Col. Smith believed the operator should feel the suspensory ligament give way before seeing the lens emerge. He believed that the operator should then act with necessary promptness and relax the extra pressure of the muscle hook in order to avoid squeezing out vitreous between the back of the lens and the scleral lip of the wound. However, "if the surgeon is heavy handed, he will not feel the

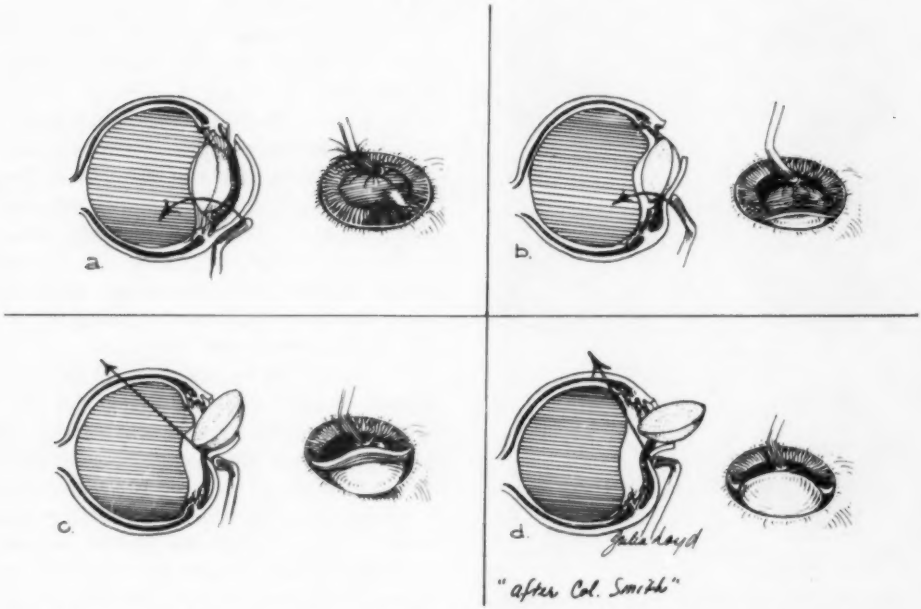


Fig. 1 (Ellis). *First Smith procedure.* (a) Lens hook over inferior cornea—drawings on right represent operating surgeon's view with inferior limbus at top of sketch. (b) Point of hook twisted backward —pushes lower edge of cataract back and causes upper edge to come forward. (c) Upper edge of lens being delivered. (d) Pushing lens completely out of eye by folding cornea behind it.

dislocation occurring, and will not relax the pressure with the necessary promptness, but will inevitably have a considerable portion of escape of vitreous in his cases."

Col. Smith believed that the dexterity necessary for this operation is obtained only by long practice and careful personal instruction from an expert. He also mentioned that in a certain small percentage of cases, the suspensory ligament is so strong, so elastic, requiring so much pressure for intracapsular delivery, that in these cases, "even expert hands will be unable to avoid some escape of vitreous."

Because of rupture of the lens capsule, especially in morgagnian and soft cataracts, Smith developed a new method of intracapsular extraction called "tumbling" (fig. 2). By tumbling Smith meant the rotation of the lower edge of the lens forward about a transverse axis so that the lower edge and not the upper edge is delivered first. He stressed that one must first dislocate the lens and detach it from the suspensory ligament before attempting to remove it from the eye. He advocated making the lens swing about some transverse axis to concentrate the strain on the suspensory ligament at one or two points. Then the lower edge of the lens is rotated forward about a transverse axis so that the lower edge is delivered first. He placed the lens hook over the cornea inferiorly as before (fig. 2-a and b). The point was then twisted back by rotating the handle of the instrument between the thumb and fingers. Then the rotation is continued until the point comes up against the resistance of the sclerocorneal "ring."

The lens hook is twisted backward and downward and pressure is exerted toward the optic nerve and also toward the patient's feet. This will dislocate the suspensory ligament inferiorly and the inferior lens rolls up under the point of the lens hook remaining

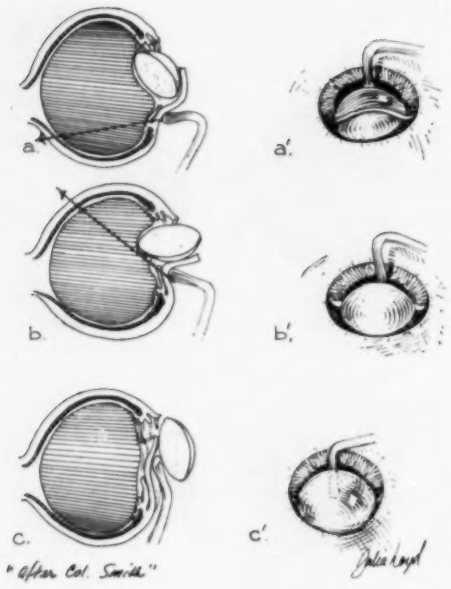


Fig. 2 (Ellis). *Smith tumbling technique.* (a) Lens hook twisted backward over inferior cornea (a′, b′ and c′ represent views as seen by operating surgeon.) (b) Inferior pole of lens is being delivered first. (c) Completion of extraction—lower pole of lens is now above the original upper pole.

attached to the suspensory ligament above at the wound entrance (fig. 2-b). The attached suspensory ligament above acts as an effective barrier to prevent the vitreous from escaping while the inferior lens is delivered.

Smith then warned that it was very essential to relax the pressure at the "psychologic moment" in order to keep from losing vitreous. Then generally keep the corneal flap pressed against the posterior surface of the emerging lens. The tucking of the cornea under the tumbling lens is continued until the lens is completely out of the eye. It helps peel off the zonular membrane and helps prevent vitreous from coming anteriorly below the inferior edge of the lens.

Col. Smith writes that he used these two methods primarily in his service in India and then, in 1921, visited the United States and Canada after his retirement. He was told by his pupils that those who did not do many cataract extractions noted frequent vitreous loss.

Smith visited Philadelphia and as many of the senior ophthalmologists remember performed cataract extractions at the Wills Eye Hospital. Those of the senior men who recalled this to me, seemed to remember most vividly two facts: (1) that Col. Smith smoked a cigar while operating, with the ashes frequently falling where they would and (2) vitreous flowed freely.

Col. Smith with his son revisited the Punjab and, in 1926, perfected a modified technique of delivering a lens intracapsularly by external pressure alone (fig. 3). He noted that, if pressure is made on the sclera over the vitreous, the vitreous being a fluid would transmit the pressure to the back of the lens and draw the lens straight forward. The resistance to the movement of the lens would be least in the middle of the incision so that the lens would present with its upper edge first.

To counteract this tendency, Col. Smith applied a smooth curved spatula with its convexity backward over the middle of the incision (fig. 3-a and a′). He would make sufficient pressure to fix the upper edge of the lens and prevent it from coming forward. The lens hook was then put on the flat over the sclera inferiorly with the heel downward and the point well behind the circumference of the lens, that is, four to five mm. behind the sclerocornea.

This instrument placed inferiorly was pressed on the vitreous toward the center of the globe. The upper edge of the lens was prevented from coming forward by the spatula and the lower edge of the lens would dislocate (fig. 3-b and b′).

When the lens dislocated inferiorly, the point of the hook was brought up onto the cornea and insinuated behind the advancing lower margin of the lens (fig. 3-c and c′). The extraction was then completed by fold-

ing the cornea behind the lens while pressure with the spoon was removed. Finally, the upper edge, to which the suspensory ligament was still attached was "raked off the wound." Vitreous escape occurred only if the surgeon kept his lens hook back on the sclera too long after the lower lens border had rolled up, according to Smith.

Col. Smith believed that this type of delivery would eliminate loss of vitreous entirely. He suggested that this method be used for dislocation of the most stubborn lens. At this time he believed that his original method for delivering the lens upright be put on the shelf in a museum for historical interest only. Smith also warned that this combined method of pressure with spoon and lens hook should not be applied to the big swollen soft cataract for fear it would be squeezed between the two instruments and the capsule break. For this latter type of cataract he advocated the original method of tumbling, that is pulling the eye downward with the point of the lens hook astride the sclerocorneal ring without assistance from any other instrument. He advocated a full incision of not less than 180 degrees.

Derrick Vail credits Smith as describing the rotary pressure method for separating the zonule inferiorly and believes that the most important and most effective maneuver is the tucking of the cornea under the tumbling lens, which Smith described.

Because of the frequency of vitreous loss, the Smith-Indian operation went out of practice and most agreed with Daniel B. Kirby who described the Smith operation as being brutal and too dangerous. Derrick Vail wrote that it is dangerous to use because it requires the use of vitreous pressure. Most ophthalmic surgeons therefore condemn Smith's method of intracapsular cataract extraction by external manipulation.

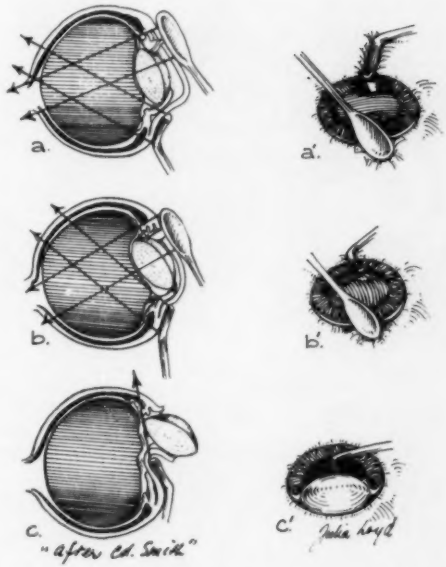


Fig. 3 (Ellis). *Smith technique of 1926.* (a) Lens hook over inferior sclera and the curved spatula over middle of incision (a', b', c' views of operating surgeon). (b) Inferior pole of lens is first dislocated. (c) Lens hook folding cornea behind inferiorly dislocated lens.

Modified Smith technique

This technique of intracapsular cataract extraction has been developed by Sir Henry Holland of India and Pakistan. The cataract is also delivered by external manipulation, although employed somewhat differently than with the Smith technique. Sir Henry Holland has described certain vital and important restrictions and limitations essential to his procedure.

The contraindications to the modified Smith cataract extraction are: (1) plethoric, short-necked, tense patient; (2) "dangerous eye," high myope; (3) glaucoma; (4) young adult, under 45 to 50 years of age; (5) evidence of positive pressure after anterior chamber is entered; (6) if "legitimate" pressure does not dislocate the lens; (7) congenital cataracts; (8) traumatic cataracts; (9) complicated cataracts.

Because of the great tendency to vitreous loss in the plethoric, corpulent, tense person, Sir Henry Holland does not recommend his operation in such patients. He also holds

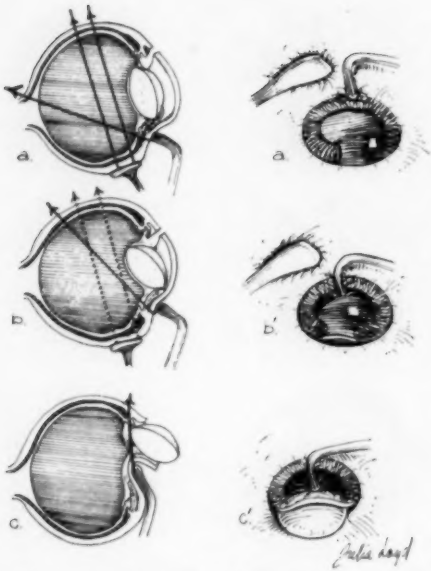


Fig. 4 (Ellis). *Modified Smith technique.* (a) Spatula exerting pressure on sclera three to four mm. from limbus inferiorly in 4- to 5-o'clock meridian, while lens hook is applied at lower limbus (a', b' and c' operating surgeon's view). (b) Pressure of spatula remains constant; direction of pressure of the hook is changed toward incision as lens dislocates. (c) Spatula is removed and lens is delivered by hook which pushes cornea against it.

firmly to this opinion in regard to so-called "ox eyes" or "dangerous eyes," for example, those in high myopes and eyes in which the upper lid cannot be lifted easily from the globe. In these instances, he advises planned extracapsular extraction. Cataracts associated with glaucoma, congenital, traumatic and complicated cataracts, as well as cataracts in young adults—are all included as contraindications to this method of surgery.

Sir Henry Holland also stresses the point that the surgeon should never say preoperatively that he "will *do*" this modified Smith operation, but rather than he "will *try*." If he has no immediate success, he should resort to forceps, erisophake, or the extracapsular technique. Thus, if "legitimate" external pressure does not succeed in dislocating the lens, some other means of extraction should be employed.

Procedure

Sir Henry Holland believes it is very important that the assistant hold the upper lid away from the globe with a retractor throughout the operation. The surgeon takes the spatula or spoon in the left hand and places the end vertically on the sclera about three to four mm. below and to the left of the sclerocorneal junction between the 4- and 5-o'clock positions (figs. 4 and fig. 5). (This is lower than Smith recommended.)

Slight pressure is exerted with the instrument until the normal convex corneal surface is seen. The surgeon then takes a blunt hook in his right hand and applies the ball end of the hook to the lower limbus and gentle pressure is made with both instruments in position (fig. 4-a and b). The spatula or spoon is kept quite stationary and used chiefly to steady the eyeball while the ball end of the hook is pressed on the lower limbus, straight backward toward the optic nerve (and feet).

Holland believes the spoon pressure raises the lens in similar fashion as does the forceps at the beginning of the forceps delivery. If the lens shows no sign of being dislocated, the ball end of the hook is moved slightly from side to side, while the spatula still is not moved and maintains slight steady pressure.

If "legitimate pressure" does not succeed in dislocating the lens, Sir Henry Holland advocates some other means of lens extraction.

As soon as the lens appears in the corneal incision, the spatula is kept in the same position while the ball end of the hook is used to follow the lens up, using side-to-side movements and now the pressure is not directed straight backward toward the optic nerve but is made in an upward direction toward the incision. After two thirds of the lens has appeared in the incision, pressure is reduced, as the lens will practically deliver itself, and the cornea is merely tucked under the lens. At the conclusion of the operation the cornea will then be in its proper place.

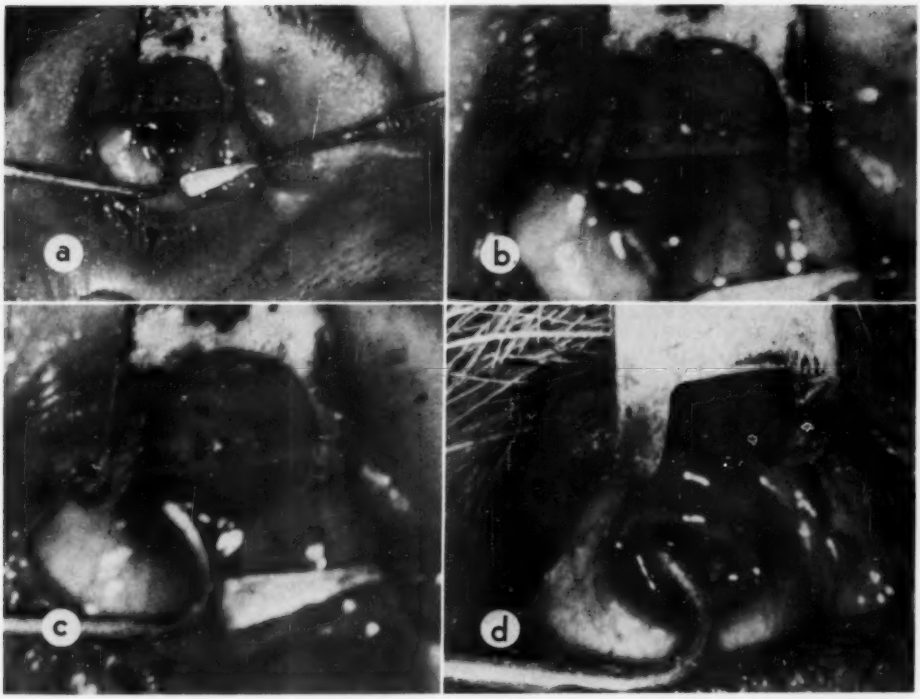


Fig. 5 (Ellis). *Modified Smith technique.* (a) Flat surface of spatula over sclera about four mm. from limbus and end of hook over lower limbus. (b) Gentle pressure is made until normal convex corneal surface is seen. (c) Spatula is kept in same position; lens hook follows up lens after it is dislocated inferiorly and spatula pressure is gradually reduced. (d) Spatula is removed; hook pressure greatly reduced and tucks cornea behind lens.

Sir Henry Holland believes that tumbling may be performed on mature, hypermature, and intumescent cataracts. "Experience will enable the operator to decide which lenses will tumble." If in doubt, the operator may first try to dislocate the lens below and, if this fails, may then try to extract in the upward method.

In tumbling the lens the pressure of the ball end of the muscle hook is made in a different position—not straight backward toward the optic nerve but downward toward the patient's feet, while the point of the hook is placed about three mm. from the sclerocorneal margin just inside the ciliary ridge. Thus, the pressure is directed toward the patient's feet. Then, as the lens begins to tumble, the operator should not release his pressure until the lens has passed the equator when he should alter the direction of his pressure and follow up the lens, pushing it upward toward the incision.

Advantages

Sir Henry Holland believes the advantages of this method are:

1. Fewer lens capsules are broken, especially when the capsule is tense.

2. No instrument touches the posterior surface of the cornea. This is especially important in endothelial dystrophy. The incidence of postoperative vitreous adhesions to the cornea may also be lowered since no instrument damages the corneal endothelium.

3. The cataract delivery without placing anything into the anterior chamber may pos-

sibly decrease the chance of postoperative infection.

Disadvantages

1. The main disadvantages is the possibility of increased chance of vitreous loss. Most ophthalmic surgeons agree that vitreous loss is probably the most disastrous complication in cataract surgery. Therefore, if there is a higher incidence of vitreous loss, this method of cataract surgery should not be employed. Sir Henry Holland and his son, Ronnie Holland, both of whom use this method of cataract surgery believe that vitreous loss is not over two percent. Having worked with these men in their Mission Eye Camp in Pakistan, I can verify this incidence.

2. The Hollands do warn that the surgeon must be more experienced for this technique than for the forceps or erisophake delivery. It should not be employed by the occasional operator. The amount and direction of external pressure used is very important and a beginner should never attempt this method.

Comment

It is obvious that one's interpretation of "legitimate" pressure is of utmost importance in this form of cataract extraction. Since alpha chymotrypsin was introduced by Barraquer, its use is gaining in popularity. This enzyme, by dissolving the zonules of the lens, has greatly facilitated cataract extraction. In many cases the surgeon merely has to remove the cataract which has already been dislocated from its zonular attachment and has come forward into the anterior chamber. In these cases lens extraction by external manipulation may be very satisfactory. Because of the use of alpha chymotrypsin, the surgeon may employ very little "legitimate" external pressure. Of course it is better to err on the conservative side and always remember the limitations of this method. Dr. David Shoch of Chicago and Dr. Masazumi Inouye of Japan have already reported satisfactory results employing external manipulation alone after alpha chymotrypsin.

Summary

A method of cataract extraction by external manipulation alone has been described. With the use of alpha chymotrypsin this means of surgery may be employed in many properly selected cases.

1711 Rittenhouse Square (3).

References

1. Vail, D.: Intracapsular extraction; mechanics, technique, variations. (Symposium on cataract extraction.) Tr. Am. Acad. Ophth., May-June, 1954.

2. Kirby, D. B.: Advanced Surgery of Cataract. Philadelphia, Lippincott, 1955, pp. 151-152.

3. Smith, H.: A new technique for the expression of a cataractous lens in its capsule. Arch. Ophth., **55**:213-224, 1926.

4. Fisher, W. A.: Senile cataracts: Methods of operating, collaboration with Fuchs, Barraquer, Smith, Holland and Wright. Chicago, Chicago Eye, Ear, Nose and Throat College, 1923.

5. Holland, H., and Holland, R. W. B.: Notes on 221 intracapsular cataract extractions performed in three weeks at Khairpur in 1947. Brit. J. Ophth., **33**:101-106, 1949.

6. ———: Personal communication.

7. Shoch, D.: Enzymatic zonulolysis. Tr. Penn. Acad. Ophth., **12**:70-72 (Fall) 1959.

8. Inouye, M.: Use of quimatrase for cataract intracapsular extraction. J. Clin. Ophth. (Japan), **13**: 565, 1959.

FAMILIAL RETINAL DETACHMENT

A. I. Friedmann, D.O.M.S., and E. Epstein, D.O.M.S.
Johannesburg, South Africa

The following familial incidence of retinal detachment is reported to add to those cases already recorded in the literature. It illustrates the following interesting features:

1. The dominant nature of the defect, as indicated by the occurrence of the disease in the two families of a twice-married woman.

2. The anticipation of the disease, as exhibited in the affected second generation.

3. The relatively small degree of myopia that occurred in most cases.

4. The common feature of retinal degenerative changes present in all those affected whom we examined.

Case histories (Fig. 1)

The ages quoted were those in 1955. I, II, 1 and 2; III, 1, 2, 3, and 4 live (d) in Scandinavia. By hearsay the eyes never caused trouble. Some used reading glasses others not.

III, 5, aged 81 years, had a mature cataract of the left eye, pupil reactions were good and projection excellent. The right eye showed phthisis bulbi. This patient was in the hospital in 1936 with a diagnosis of corneal abscess.

IV, 1, aged 58 years. Fundi were normal; emmetropic.

IV, 2, aged 55 years. In 1949 there was a detached retina in the left eye. A rather advanced cataract obscured details. Two operations were unsuccessful. The right eye showed peripheral degenerative changes above and below. Vision was: R.E., −3.5D. sph. ⊃ −1.0D. cyl. ax. 180° = 6/6; L.E., −3.0D. sph. ⊃ −2.0D. cyl. ax. 165° (taken from old glasses). By 1955 vision in the right eye was reduced to 6/24 with a −7.0D. sph. ⊃ −1.0D. cyl. ax. 165°, because of lens sclerosis and macular degeneration.

IV, 3, aged 53 years, had a detachment in the right eye in 1943. Operation was unsuccessful and the eye was subsequently enucleated: Vision, L.E., was then 6/18 with a −0.5D. sph. ⊃ −1.75D. cyl. ax. 80°. No fundus record was available. In 1945, the left eye developed a detachment. Operation was unsuccessful.

IV, 4, aged 51 years, had normal fundi. Vision in each eye was 6/6 with a −0.5D. sph. ⊃ −0.25D. cyl. ax. 180°.

IV, 5, aged 49 years, in 1946 after a trivial injury (foreign body on cornea from grindstone) noted defective left vision. There was a shallow extensive detachment of the lower outer quadrant involving the macula. Operation was successful. There was peripheral retinal degeneration in both eyes as well as early cataracts. Vision was: R.E., with a −0.75D. sph. ⊃ −0.5D. cyl. ax. 90° = 6/6; L.E., with a −0.5D. sph. ⊃ −0.5D. cyl. ax. 90° = 6/6p. By 1952 the right cataract was mature and the left very advanced. After extracapsular extraction from the left eye vision was 6/6 with a +9.0D. sph. ⊃ +2.5D. cyl. ax. 160°. Although the cataract in the left eye has been ready for surgery for several years he has deferred operation for domestic reasons.

IV, 6, aged 37 years, spontaneously developed a detached retina in the right eye in 1943 while on active service. Operation was successful but some years later the retina detached again and this eye is now blind. No records of refraction or fundus examination are available, and he cannot be traced.

IV, 7, cannot be traced.

V, 1, aged 32 years, developed detachment in the right eye in 1936. Operation was unsuccessful. Vision, L.E., with a −0.75D. sph. = 6/6. This patient developed a cerebral glioblastoma which caused his death in 1955.

V, 2, aged 30 years, fundi were normal, emmetropic.

V, 3, aged 28 years, fundi were normal. Vision was: R.E., with a +0.5D. sph. ⊃ +0.75D. cyl. ax. 160° = 6/5p; L.E., with a +0.75D. cyl. ax. 170° = 6/5p.*

V, 4, aged 24 years, developed a spontaneous detachment in the left eye in September, 1948, with peripheral holes at the 2, 5, and 6-o'clock positions. Operation was successful and vision, L.E., with a +1.0D. sph. ⊃ −1.5D. cyl. ax. 165° = 6/18. Both retinas showed degenerated areas. In December 1948, the patient slipped and jarred the head. A detachment was now found in the right eye with three holes in the upper temporal quadrant. Operation was successful and vision, R.E., with a −0.25D. sph. ⊃ −1.5D. cyl ax. 150° = 6/18.

V, 5, aged 21 years, had normal fundi. Vision was: R.E., with a −0.25D. sph. ⊃ −1.0D. cyl. ax. 180° = 6/6; L.E., with a −1.0D. sph. ⊃ −1.0D. cyl. ax. 165° = 6/6.

V, 6, aged 18 years, had normal fundi. Emmetropic. Vision, O.U., was 6/6.

V, 7, aged 13 years, in 1949, had vision of: R.E., with a −3.5D. sph. = 6/18; L.E., with a −6.5D. sph. = 6/18. In 1953: R.E., with a −4.5D. sph. = 6/18; L.E., with a −8.5D. sph. = 6/18. Both fundi

* This patient has recently been examined—she had not been seen for some years previously to this. She now has a marked but localized area of chorioretinal degeneration up and out at the equator of each eye. These areas will be treated by light coagulation.

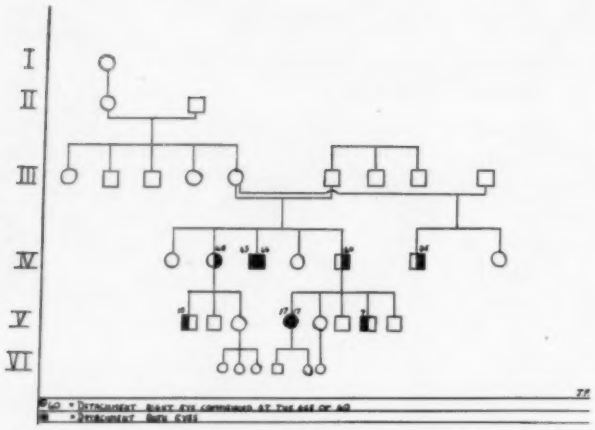


Fig. 1 (Friedman). Pedigree of family reported.

show retinal degeneration. In 1954, this patient developed a large detachment in the right eye. Diathermy alone was unsuccessful but subsequently diathermy and a scleral overlap were successful. In 1955, vision was: R.E., with a −4.5D. sph. ⊂ −1.0D. cyl. ax. 90° = 6/24; L.E., with a −9.5D. sph. = 6/24. In 1957, R.E., with a −5.0D. sph. ⊂ −0.5D. cyl. ax. 90° = 6/18p; L.E., with a −9.5D. sph. = 6/18.

V, 8, aged nine years had normal fundi. Vision was: R.E., with a −2.5D. cyl. ax. 75° = 6/9; L.E., with plano = 6/9.

VI, 1, aged eight years, had normal fundi. Emmetropic. Vision was, O.U., 6/6.

VI, 2, aged six years, had normal fundi. Emmetropic with vision, O.U., 6/6.

VI, 3, aged three years, had normal fundi. Emmetropic.

VI, 4, aged two and one-half years, under cycloplegia was found to be emmetropic.

VI, 5, aged one year, under cycloplegia showed +0.5D. sph., R.E., and +1.5D. sph., L.E.

VI, 6, aged one year, had normal fundi and under cycloplegia showed a small (H).

Discussion

From Figure 1, it can be seen that the inherited defect first manifested itself in generation IV and appeared in four eyes in patients between the ages of 40 to 48 years. Among the offspring of the carrier's second marriage a detached retina occurred in one eye of a person aged 25 years. In the next generation it appeared in four eyes of persons between the ages of 11 and 17 years, thus showing marked anticipation.

Table 1 tabulates the degree of myopia in the cases that developed retinal detachment. A blank indicates that it was impossible to refract that eye or obtain a previous refraction. A relatively high myopia occurs in one case; a moderate degree in another, and in the rest is slight. Three others in the family also showed small degrees of myopia. It thus appears that the degree of myopia and the tendency to detach are unrelated.

The four cases that were personally examined and treated showed bilateral peripheral choroidoretinal degeneration of a nonspecific type and not related to the degree

TABLE 1

Myopia in cases developing retinal detachment

	Right Eye		Left Eye	
IV, 2	−3.5D. sph. ⊂ −1.0D. cyl. ax. 180°		Detach.	−3.0D. sph. ⊂ −2.0D. cyl. ax. 165°
IV, 3	Detach.		Detach.	−0.5D. sph. ⊂ −1.75D. cyl. ax. 80°
IV, 5	−0.75D. sph. ⊂ −0.50D. cyl. ax. 90°		Detach.	−0.5D. sph. ⊂ −0.5D. cyl. ax. 90°
IV, 6	Detach.			
V, 1	Detach.			−0.75D. sph.
V, 4	Detach.	−0.25D. sph. ⊂ −1.5D. cyl. ax. 150°	Detach.	+1.0D. sph. ⊂ −1.5D. cyl. ax. 165°
V, 7	Detach.	−4.5D. sph.		−9.0D. sph.

of myopia. The circular retinal holes found in these four cases, with opercula in the vitreous, indicate the existence of vitreo-retinal adhesions, and the mechanics of the detachment.

It is of interest in this family that only one adult (IV, 4) is myopic and did not develop a retinal detachment. The degree of myopia is very small (-0.5D sph. $\bigcirc -0.25$D. cyl. ax. 180° in each eye). This case also had no retinal degeneration. The children who are myopic will be followed as far as possible into later life to see whether retinal degeneration without or with retinal detachments develop.

Similar families have been described before and, in fact, in the general population this tendency of retinal detachments occurring more frequently in myopic eyes is well known. Whether in this family the myopia and the retinal degeneration are linked in the same gene, or in closely associated genes, is mere speculation, but the reality of the linkage is undoubted.

The other unanswered problem is whether, in the general population, retinal degeneration (of the type tending to lead to retinal detachments) and myopia are linked in a similar way and, if so, whether this myopia is of a particular type, such as axial as compared to refractive myopia.

Summary

A pedigree of retinal detachment is presented. The defect appears to be dominant and was introduced into the two families of a twice-married woman. The relationship between retinal degeneration and myopia is discussed.

301 Medical Centre, Jeppe Street.

We wish to express our appreciation to Dr. Alexander Jokl and to the D.G.M.S. War Records for information made available to us.

References

Duke-Elder, S.: Textbook of Ophthalmology. London, Kimpton, 1940 v. 3, p. 2867.

Levy, J.: Brit. J. Ophth., **36**:11, 1952.

Sorsby, A.: Genetics in Ophthalmology. Butterworth, London, 1957, p. 180.

METHODS FOR THE SEPARATION OF LIDS IN CATARACT SURGERY*

Paul U. Fechner, M.D.

Eloise, Michigan

At the end of the last century Czermak[1] remarked that a lid speculum "should be light, should not hamper the hand or instruments of the surgeon, it should be easily removable, preferably with one hand, and without exertion of pressure on the eye." In 1922, Elschnig[2] repeated these specifications. However, the subject of separation of the lids for surgery on the globe, and particularly intraocular surgery, has apparently not been discussed in detail. This is surprising as in a number of procedures, for instance in cataract surgery, a suitable method of separation of the lids is a factor of outstanding importance for the success of the operation.

This paper concerns itself with advantages and disadvantages of methods of lid separation applied in cataract surgery, and particularly with those criteria that best provide freedom of action for the surgeon and safety from vitreous complications. The term "method" of lid separation is indicated because such different devices as sutures, hooks and specula will be discussed.

* From the Department of Surgery, Section of Ophthalmology, Wayne County General Hospital.

I. Introduction

Czermak's demands of a lid speculum may be re-defined to suit the purpose of this paper:

It is desirable that any method for the separation of the lids should:

1. Give retraction of the lids.
2. Not impair the work of the surgeon.
3. Be effective without manual help, that is, leave the hands of the surgeon and the assistant free.
4. Not exert pressure upon the eye.

These are classic demands, they are generally accepted and their rationale is clear. They assure freedom of action to the operator and serve the prevention of vitreous complications. However, the presence of three additional features is extremely useful. The method for separation of the lids should also:

5. Permit lifting of the lids from the eye.
6. Permit lessening of the width of the palpebral opening.
7. Permit both these movements to be performed by the assistant with one hand, and so gently that the surgeon can continue with the operation proper.

In essence then, the lid separation should not be rigid but permit adjustment during operation in both the frontal and saggital plane without impairment of the surgeon's work.

This adjustment can considerably mitigate the danger of vitreous prolapse. Bulging vitreous is usually due to outside pressure upon the eye. It may be caused by undue handling of instruments, by the weight of the lid speculum, by venous congestion of the orbital contents—for instance when the patient coughs—by retrobulbar hemorrhage, or by incomplete akinesia. It is obvious that in any of these complications elevation of the lids, or of the speculum and the lids, will alleviate the danger. It is also obvious that it will be of advantage to maintain this state of relief long enough for the surgeon to remove the lens and close the corneo-scleral wound. These are the reasons for the postulates 5 and 7.

The sixth postulate—that in certain cases the approximation of the lids, or branches of the speculum, is needed—may require some explanation. Two different situations have to be considered.

One is the case of incomplete akinesia. If the patient attempts to close his lids in such condition, and if this movement is forcibly prevented by a lid speculum or lid sutures, the innervation may spread from the orbicularis muscle to the external eye muscles as in Bell's phenomenon. It would then be necessary to lift the lids in order to counteract the orbicularis muscle. However, in addition, it may be very useful to prevent the spreading of innervation by letting the orbicularis muscle succeed to some extent, that is, to permit a controlled degree of lid closure.

The other situation can occur only when a lid speculum is used. Occasionally it is not possible to elevate the branches of the instrument without their previous approximation. The reason is that the blades in a state of maximal separation are caught by the tight fibrous structure of the palpebral aperture (in the absence of lateral canthotomy) or by the orbital rim (fig. 1-a and b).

Although it appears logical to embody into the method of lid separation for cataract surgery means to cope with the danger of vitreous complications, it will be seen that such provisions are insufficient or absent in a number of methods currently in use.

II. Methods of lid separation

1. Lid hook

In India disciples of Smith are still using the lid hook, usually a squint hook.[3] The assistant lifts the upper lid away from the globe with the hook. He pulls the lower lid down with the thumb of the other hand and presses it against the maxillary bone. The assistant uses both hands. Requirement 3 is not fulfilled.

2. Lid sutures

Usually two sutures are inserted near the margin of the upper lid and the two nasal and temporal ends are fixed to the drape. One suture only is applied to the lower lid (fig. 2-b).

Maximum opening of the palpebral aperture can be achieved, no instruments hamper the surgeon, and the hands of the assistant remain free. Counterbalancing these advantages, however, is the fact that as the margins of the lids become elevated by traction of the sutures, the attached borders of the tarsal plates of the upper and lower lid may become pressed against the globe (fig. 2-a and b). Under normal conditions this pressure is weak and probably does not exceed the pressure exerted by lid specula of the unsupported type (see later).

The latent danger of the arrangement can, however, manifest itself under the menace of vitreous prolapse. In an attempt to eliminate all pressure upon the eye the surgeon may try to lift the lids from the globe by traction on the sutures. The move will bring difficulties in two respects. To pull all three sutures simultaneously involves surgeon and assistant and prevents the partners from continuing the operation proper. Much worse is that while the margins of the lids are being pulled away the attached borders of the tarsal plates may press against the globe with increased force.

Similarly, when a patient with incomplete akinesia squeezes, the lid margins will be pulled away from the eye and the attached border of the tarsal plates be pressed against it.

When these complications arise suddenly, one is helpless. If there is time the situation can be saved by gently introducing a squint hook under the upper lid and pulling the lower lid downward.

The method of lid separation by sutures, therefore, meets the demands of 1 to 3 well. However, it does not satisfy the requirements 4, 5, 6, and 7. The method is advantageous whenever it is difficult to insert a speculum, that is, in certain cases of scarred conjunctiva with shrunken fornices, narrow palpebral aperture, or with symblephara. It appears wise to confine its use to this indication. When the method is used one should

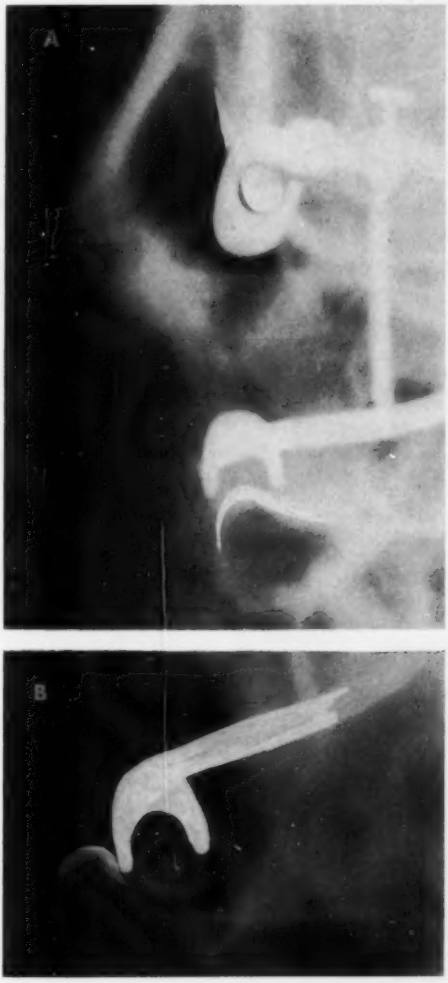


Fig. 1 (Fechner). *Lid speculum in position,* branches maximally separated. (A) Blades grasping around upper and lower orbital rim. (B) Lower blade inside orbita. It is obvious that from neither of these positions can the lid speculums be elevated without previous approximation of the blades. (Retouched X-ray photos.)

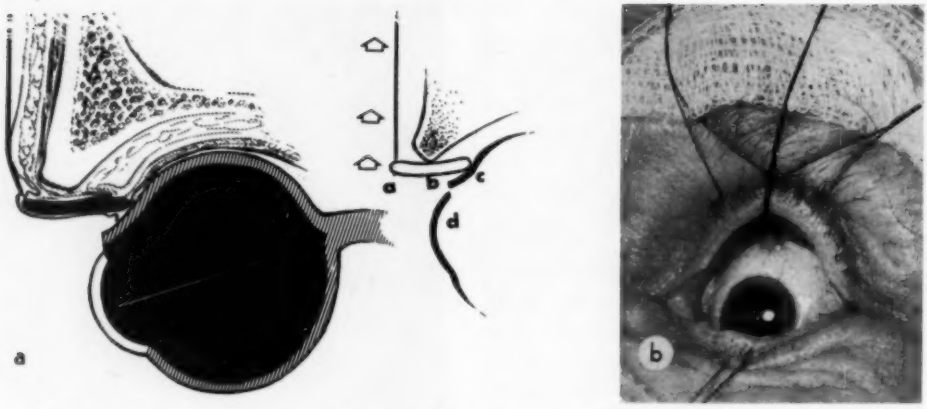


Fig. 2 (Fechner). *Lid sutures in place.* (a) Semidiagrammatic and diagrammatic. The tarsal plate is being pulled against upper orbital rim which acts as fulcrum. The attached (proximal) border of the tarsal plate is pressed against the globe creating tendency for gaping of wound and bulging of vitreous. (b) The proximal end of upper tarsal plate is seen to press against globe. At 12-o'clock position is bridle suture. Same patient as in Figure 6.

be conscious of its particular hazards and provide adequate akinesia and sedation.

3. Simple lid speculum (sliding type)

The instrument is exemplified by Murdoch's and Mellinger's specula (fig. 3-b and 3-c). The spring, when present, is not strong. The instrument is locked by pressure which the lids exert when the palpebral aperture is distended.

If the instrument is light the first three postulations are well met, and also, to a lesser extent, the fourth. However, no gentle narrowing of the branches with one hand is possible. The desirable features of demands 6 and 7, therefore, are completely absent.

4. Simple lid speculum (spring type)

An example is the old speculum of Smith (fig. 3-a). The two branches of the instrument have a common joint and are kept apart by a spring. There is no locking mechanism. The branches of Smith's speculum are short so that the joint rests over the zygomatic bone close to the orbital rim.

Provided the instrument is of light weight and has a strong spring, the first three, and to a lesser extent the fourth, demands are fulfilled. Again, as with the sliding type of the simple lid speculum, the sixth and seventh demands are not satisfied. First, it is difficult to grasp the instrument without pushing the globe. Second, although the assistant might manage to lift the speculum from temporally without hampering the surgeon, he will hardly be able to narrow the shafts from this position. He would have to grasp the instrument from above and thereby occupy space that the surgeon needs for the continuation of the operation (fig. 4).

5. Simple lid speculum with spring and lock

The branches are kept separated by a spring. In addition, a locking mechanism is present, usually a screw. An example is William's instrument (fig. 3-d).

The demands 1 to 3, and perhaps 4, are fulfilled, yet the instrument leaves much to be desired with regard to the requirements 5, 6, and 7. As already pointed out, to have the instrument locked may at times aggravate the situation when the patient squeezes.

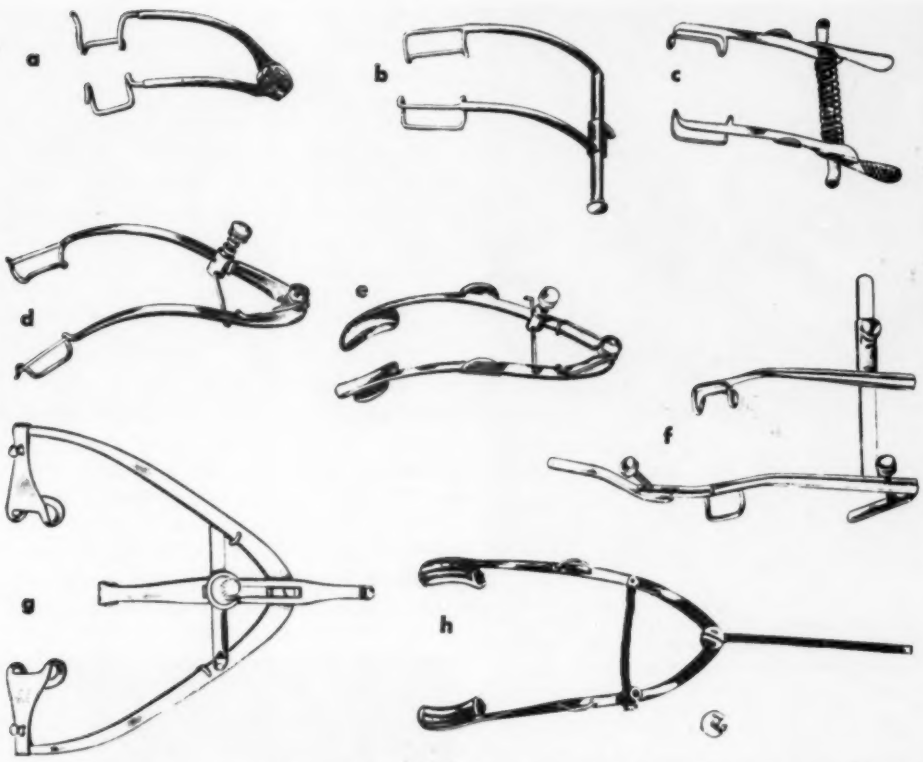


Fig. 3 (Fechner). *Types of lid specula.* (a) Simple (unsupported) lid speculum—spring type (Smith). (b) Simple lid speculum—sliding type (Murdoch). (c) Simple lid speculum—sliding type (Mellinger). (d) Simple lid speculum with spring and lock (Williams). (e) Simple lid speculum with spring and lock (Lister-Burch). (f) Lid speculum with lock—supported by legs (Arruga). (g) Lid speculum with lock —supported by orbital rim (Guyton-Park). (h) Simple lid speculum with thorn. Screw of lock is removed and lying aside instrument (Fechner).

Approximation of the branches is possible only after the instrument is unlocked which requires two hands to do it with care. Furthermore, it is almost impossible to elevate and narrow the instrument without hampering the surgeon.

6. Lid speculum with lock (supported by legs)

The weight of these instruments, for instance Arruga's (fig. 3-f), is transmitted to the root of the nose and to the temporal orbital margin. The palpebral aperture is kept distended by a locking mechanism.

This type of instrument does not press on the eye and even keeps the lids slightly elevated. The pressure which the bridle suture exerts on the upper branch is not transmitted onto the globe as frequently is the case with simple lid specula[4] and lid sutures. This instrument, therefore, offers great advantages over simple specula. However, it is still more difficult than with simple specula to narrow the branches and lift the instrument. The need for this adjustment might arise in poor akinesia or when the patient is restless, even though a supported type of speculum is used.

The classic demands 1 to 4 are excellently satisfied, but the instrument permits no

Fig. 4 (Fechner). *Simple lid speculum in place.* Assistant attempts to approximate the blades. The instrument is grasped from above so that the small finger counterbalances the pull exerted by the lids on the blades. This position of the hand decreases the space available to the surgeon.

handling during operation as asked for under demands 5, 6, and 7.

7. Lid speculum with lock (supported by orbital rim)

The Guyton-Park instrument (fig. 3-g) is the only instrument of this type known by me. The weight of this speculum is not supported by the eye but by the orbital rim on which rest long extensions of the blades and the shafts. The shafts are kept apart by a locking mechanism.

Unless the eye is fairly prominent no pressure is exerted on the globe and the lids are slightly elevated from the bulbus. The demands 1 to 4 are completely fulfilled. However, the structure of the instrument and particularly the fact that the blades hinge loosely on the shafts make it virtually impossible to elevate the lids further to allow their approximation. In deeply set eyes the operative field is smaller than with other instruments (fig. 6). In patients with very prominent eyes difficulties arise from the fact that the blades cannot be elevated beyond the level of the orbital rim.

Nevertheless, in the presence of normal anatomic conditions and sufficient akinesia this lid speculum is very valuable. It should be avoided when the eyes are deeply set or prominent.

8. Modification of simple lid speculum

My modification of a simple lid speculum has solid blades and carries small handles on both branches (fig. 3-h). Temporally it possesses a thorn of approximately four cm. in length. There is no locking mechanism and, in order to effect good opening of the palpebral aperture, the spring is strong.[5] To elevate the instrument and to diminish the lid separation the speculum can be grasped gently from temporally by the assistant.

Fig. 5 (Fechner). *Fechner's instrument in place.* Assistant attempts to approximate the blades. Instrument is grasped from the side, balanced by the palm of the hand. There is almost no decrease of the space available to the surgeon.

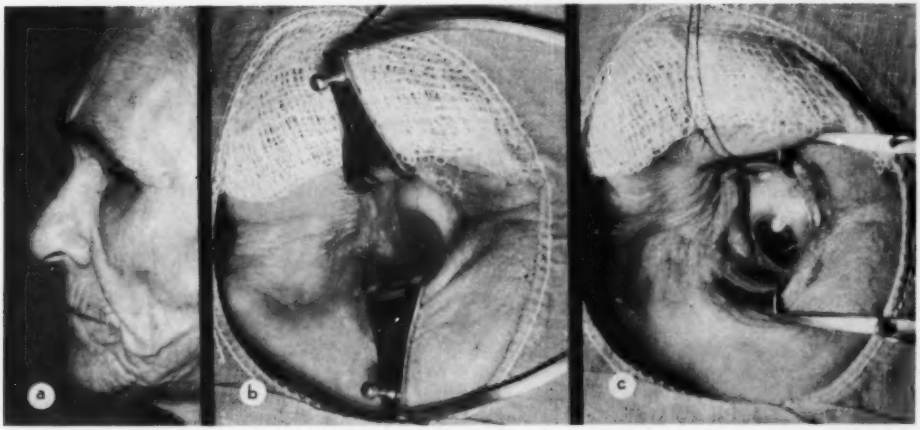


Fig. 6 (Fechner). (a) Patient with deeply set eyes. (b) Same patient as in (a) with Guyton-Park speculum in place. (c) Same patient as in (a) with simple speculum in place. It is obvious that the operative field is considerably larger with the use of a simple speculum in deeply set eyes.

The thorn will rest against the palm of the hand and prevent the instrument from tilting against the eye when it is lifted (fig. 5).

The instrument permits extremely gentle handling by the assistant with one hand. It may be elevated and the branches narrowed almost without any interference with the surgeon's work. The opportunity to handle critical situations outweighs the fact that the instrument may exert gentle pressure on the globe when not elevated because this pressure can be removed whenever desired.

Thus the demands 1 to 3 are well fulfilled, less so the fourth. Requirements 5 to 7 are better fulfilled than by any of the aforementioned methods.

The same features of easy adjustability during operation are provided by some simple specula of the spring type with long branches carrying handles, under the condition that the locking mechanism is not used. A good example is the Lister-Burch speculum (fig. 3-e). Other instruments can be bent into the required shape. The important point is that the shafts are bent strongly toward the ear of the patient thus permitting the assistant to handle the speculum from temporally without impairing the surgeon.

III. Conclusion

In the preceding paragraphs a number of different methods of keeping the palpebral aperture open during cataract surgery were discussed. Their advantages and disadvantages were pointed out.

The subject bears considerable practical importance. It is necessary for the surgeon to recognize the cases for which the method of lid separation he generally prefers is not suitable. For instance, he may have to abandon the Guyton-Park speculum for a simple type in order to gain a larger operative field on a deeply set eye. A shrunken conjunctiva due to ocular pemphigus or trachoma may require lid sutures instead of a lid speculum. The surgeon using the Arruga or the Guyton-Park speculum will have to prepare the akinesia carefully. If he prefers lid sutures he likewise will take pains to provide excellent akinesia, particularly of the orbicularis muscle. In addition, he is well advised to have a squint hook at hand and to instruct the assistant in advance in its use in case of an emergency.

Although it is emphasized that the method of choice depends on the individual case, it is felt that my modification of a simple lid

speculum offers the greatest adjustability to the varying conditions encountered in cataract surgery.

IV. Summary

Various methods for the separation of lids in cataract surgery are described. They include lid sutures, simple (unsupported) and supported lid specula and my modification of a simple lid speculum. Their usefulness is discussed, particularly with regard to the prevention of vitreous complications. Reasons are presented to show that the method of lid separation should permit adjustment during operation in both the directions of elevation and approximation of the lids. It should be possible that this adjustment be made by the assistant without impairment of the surgeon.

Section of Ophthalmology,
Wayne County General Hospital.

References

1. Czermak, W.: Die augenaerztlichen Operationen. Wien, 1893, p. 27.
2. Elschnig, A.: Augenaerztliche Operationslehre. In Handbuch der gesamten Augenh., Berlin, Julius Springer, 1922, p. 20.
3. Fechner, P. U.: Die Entbindung der senilen Katarakt durch Expression. Klin. Monatsbl. f. Augenh., **133**:71, 1958.
4. Purvis, V.: Surgical Minutiae. Tr. Ophth. Soc. U. Kingdom, **63**:302, 1943.
5. Fechner, P. U.: Zur Technik der Kataraktextraktion. Ophthalmologica, **137**:377, 1959.

THE INACTIVATION OF HERPES-SIMPLEX VIRUS BY CHEMICAL AGENTS*

Theodore W. Sery, Ph.D., and Francis P. Furgiuele,† M.D.
(With the technical assistance of Arturo Padron)
Philadelphia, Pennsylvania

Introduction

The visual impairment and disability resulting from viral infections of the cornea present a challenge to investigators in the field of ophthalmology. There is to date no known antiviral antibiotic or chemotherapeutic agent effective for man or animal in vivo.[1,2] Most important among viral infections of the cornea are the acute and chronic infections caused by herpes-simplex virus.

This work is concerned with the testing of chemical agents for their in vitro antiviral properties against herpes simplex, and for possible in vivo antiviral activity as they affect the rabbit eye. Advantage was taken of two factors: (a) the ease of quantitating herpes simplex on the chorioallantoic membrane of fertile eggs by means of pock (plaque) counting, and (b) the similarity of the infection produced on the rabbit cornea to its human counterpart. These offered the opportunity to observe directly the effects of topical administration of potent antiviral agents which might be limited for systemic use in other viral diseases by virtue of their toxicity. Those agents found to possess a high degree of antiviral activity when tested against extracellular virus would be used for in vivo trials on the rabbit cornea. The possibility that a useful compound with low anti-

* From the Department of Research, Wills Eye Hospital. This investigation was supported in part by research grants 2B-5076(C)4, B-1516, and BT-379 from the National Institute of Neurological Diseases and Blindness, National Institutes of Health, Public Health Service, Bethesda, Maryland.

† Present address: Department of Ophthalmology, Temple University Medical Center.

Acknowledgments

We wish to express our appreciation to the Fisher Scientific Company, King of Prussia, Pennsylvania, for donating most of the chemical agents evaluated in this project. We are also grateful to Dr. Samuel Askovitz for analyzing the data in this study for statistical relevance.

viral but high physiologic activity against host cells might be overlooked by this procedure has been considered. Major emphasis was given, nevertheless, to those compounds which are directly virucidal or virustatic.

The compounds were first selected for in vitro trials by design as well as by a random procedure that would permit evaluation of a wide variety of functional groups in organic compounds. Among the few compounds that have been found to be highly active against herpes simplex, a new class of virucidal agents has been revealed. This group is comprised of p-benzoquinone and some of its derivatives. In view of the fact that this group comprises large numbers that occur in a variety of biologic sources, added emphasis has been given to them as a rich source for new antiviral agents. In addition the finding that the silver ion (as silver nitrate) has an unusually strong virus inactivating property has opened an area for future evaluation of this compound as a cauterizing agent in human infections.

Materials and Methods

In vitro test method

A simple but sensitive method, modified from the one used by Burnet and Lush,[3] was used for the assay of a given compound's ability to inactivate extracellular herpes simplex virus. The relative activity of different compounds was measured by the least effective concentration needed to inactivate the virus. Virus was grown on the chorioallantoic membrane of embryonated eggs. The HF strain of egg-adapted herpes-simplex virus, kindly provided by Dr. McNair Scott of Children's Hospital, Philadelphia, was used throughout this study.

The eggs are prepared by washing the blunt ends with a suitable disinfectant such as Wescodyne or Zephiran, removing the shell over the air sac at this end with a pair of scissors, and gently peeling off the shell membrane adhering to the chorioallantoic membrane. As mentioned briefly in an earlier paper,[4] the following of certain specifications insures a high rate of survival of eggs after inoculation and also establishes conditions for reproducible quantitative data. These specifications are as follows:

1. The shell and shell membrane is removed from 12-day-old eggs and the eggs returned to the incubator; 11-day-old eggs are not used because they are not as resistant to trauma.

2. When peeling off the shell membrane it is first wetted with 25-percent glycerine to facilitate removal and to minimize trauma to the chorioallantoic membrane.

3. Opened eggs are incubated for one day to permit recovery from trauma and absorption of allantoic fluid and/or blood plasma from the chorioallantoic membrane surface.

4. Eggs are then inoculated (when 13-days old) using 0.1 ml. amount of virus suspension. The latter volume is small enough for the fluid to be absorbed before virus multiplication occurs; new virus would otherwise "float" to new sites and give false results.

5. Incubation is carried out at 35-36°C. in a moist chamber. The open end of eggs may be conveniently covered with a one ounce cap (Jos. E. Frankle Co., Philadelphia) or a glass staining dish (catalogue No. 9189, Arthur Thomas Co., Philadelphia).

The inoculum is prepared by grinding two infected chorioallantoic membranes (that is one chorioallantoic membrane is the amount of tissue that can be cut out from the exposed tissue, about 35 mm. in diameter) in a sterile mortar with alundum abrasive. The residue is taken up in 1.0 ml. of a diluent (hereafter termed BGL) containing 0.01 M phosphate buffer, 0.85-percent saline, 0.5 percent gelatin and 0.01 M lysine and penicillin-streptomycin, 50u. μg/ml. Lysine was incorporated because it inhibits phosphatase, a virucidal enzyme against herpes simplex.[5] The supernatant fluid after centrifugation constitutes the "undiluted" virus suspension; from this, 10-fold dilutions in BGL are made up to a 10^{-4} dilution. The

10^{-4} virus suspension is used as the inoculum for testing chemical agents. It usually has a virus content such that when mixed with an equal volume of BGL and incubated at 35-36°C for one hour, 0.1 ml. will produce from 100 to 1,000 pock-forming units on the chorioallantoic membrane. The best working range for obtaining reliable data is to have this number fall within 250 to 500 and this is where it most often does occur.

Values above 200 pock-forming units become uncountable due to crowding and confluency of the pock marks on the chorioallantoic membrane. A 20-percent survival of virus from a 1,000 pock-forming units inoculum or greater, it can be seen, is near the upper limit of countability and therefore masks results. Values below 100 pock-forming units are too low to allow statistical dependability of counting values when a substantial fraction of virus has been inactivated.

In this study a given chemical agent was tested for possible virus inactivating properties by preparing suitable dilutions in BGL diluent, mixing with the 10^{-4} virus inoculum (0.3 ml. each), incubating for one hour at 35-36°C followed by inoculating the chorioallantoic membrane of prepared eggs (0.1 ml. to each of three to five eggs).

For those compounds that were weakly soluble in water or BGL, suitable solutions could be had by preparing primary solutions in alcohol, acetone, or ether, from which further 10-fold dilutions in the regular diluent were possible and in which the final pH was between 6.5 and 7.5. Occasionally special diluting procedures were obtained from the Merck Index. Control runs were made to test the antivirus effect of these solvents. In those instances (as with heavy metals) where a given compound would cause precipitation of the gelatin constituent of BGL, this problem was minimized by carrying dilutions up to 10^{-2} M in water and using BGL for the succeeding dilutions.

Inoculated eggs were incubated for two days after which the exposed chorioallantoic membranes were snipped out, placed in petri dishes and the pocks counted. Controlled countings were made by determining the virus content of the inoculum. In this instance BGL was used in place of the chemical agent, mixed with 10^{-4} virus, incubated one hour and then 10^{-4}, 10^{-5}, 10^{-6} dilutions prepared for inoculation of control eggs. In Figure 1, a typical run is illustrated, showing the total virus-inactivating effect of chloramil (2, 3, 5, 6-tetrachlorobenzoquinone) at 10^{-5} molar concentration. Accompanying

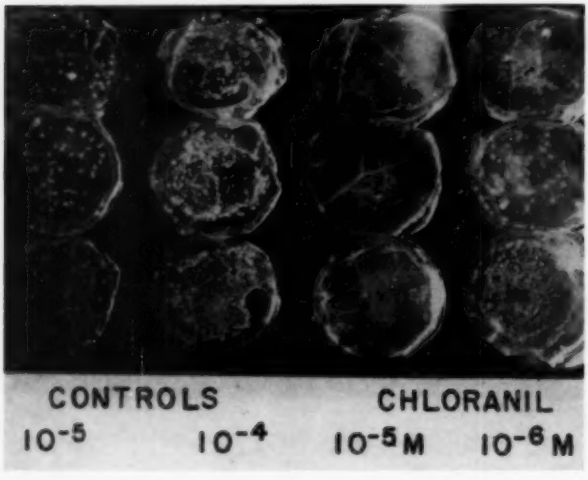


Fig. 1 (Sery and Furgiuele). Chorioallantoic membranes two days after inoculation with herpes-simplex virus. Virus at 10^{-4} dilution was mixed in equal proportion with the compound chloranil (2,3,5, 6-tetrachlorobenzoquinone) and incubated one hour at 35-36°C.; inoculations were then made on 13-day eggs. Total inactivation by chloranil occurred at 10^{-5}M concentration but not at 10^{-6}M. Controls treated with buffer instead of the chemical are shown in the two left hand columns.

controls show the virus inoculum at 10^{-4} dilution and its countable counterpart at 10^{-5} dilution.

In vivo test method

Those chemical agents found to be highly active at high dilution in vitro were selected for in vivo testing. Treatment consisted of trying to prevent the development of infection or to curtail or arrest its progress once it became established.

The standard procedure used was:

1. Rabbits were inoculated on both corneas which were previously anesthetized with one-percent pontocaine and lightly scarified by 12 crosshatch scratches on the corneal epithelium; the virus concentration, when 2×10^6 pock-forming units per 0.02 ml., would give a good series of dendritic ulcerations on the cornea in numbers sufficient to permit attempted therapy. Based on a previous study[4] this value corresponded to 200 times the virus dose necessary to produce minimal infections in 100 percent of the corneas.

2. One hour following the inoculation, treatment was instituted. It has been our finding after much experience with herpetic keratitis in the rabbit that a one-hour incubation period permits sufficient viral invasion into the cells so that dendritic ulceration uniformly occurs within 36 to 48 hours regardless of treatment that is then instituted with currently known antiviral chemicals. This also gives an added advantage in that time is gained on the herpetic ulcer, permitting two more days (the usual incubation period with the HF strain virus) for observations of the development, or nondevelopment, of the expected ulcer. In some instances longer incubation periods were also tried.

3. Topical application of the test material dissolved in a suitable vehicle was applied every five minutes for one hour in drop form. This was done one hour post inoculation and was repeated after 24, 48 and 72 hours. Toxicity trials for all agents tested were made prior to treatment of herpetic ulcers to permit the use of the highest subtoxic dose which would have no deleterious effect on corneal tissues.

4. In all cases the right eye received treatment and the left eye of the same animal was used as a control. The observation of hundreds of infected rabbit corneas inoculated in groups with an identical virus concentration has convinced us that there is wide variation in the degree of corneal involvement in two eyes of the same and different rabbits. The grading of corneal ulceration in terms of plus 1 to 4 as described by others[6,7] has, therefore, been avoided. We have instead adopted an "all or nothing" qualification when attempting to evaluate the effects of these antiviral agents. A reservation could perhaps be made if a wide difference in treated and control infections occurred consistently for a given compound.

Results

In vitro inactivation of virus

Over 150 compounds were studied for direct antiviral activity and the greater proportion were found to have little or no effect on the virus. Tables 1, 2, and 3 include data only for the more active compounds as well as for some chemicals of special interest. The other agents are summarized at the end of this section.

In the following tables the activity of the chemical agents at different concentrations is given as the percent inactivation of a given virus inoculum. Concentrations decrease toward the right and antivirus activity is, therefore, most significant for compounds that have near 100-percent values at the lower concentrations. An arbitrary end-point selected at 90 percent virus inactivation is able to accommodate any wide variation in pock counts in identically inoculated eggs.

Table 1 gives the virus inactivating values of a number of metallic cations. Those listed represent the most active of the 36 that were tested. Most prominent in the table were silver and mercury, which, at the extremely low concentration of 10^{-5}M, were able to

TABLE 1

VIRUS INACTIVATION BY CATIONS OR CATIONIC COMPLEXES

Chemical Agent	Percent Virus Inoculum Inactivated			
	Concentration* of Chemical Agent (molarity)			
	10^{-2}†	10^{-4}	10^{-5}	10^{-6}
$AgNO_3$	100	100	100	0
$HgCl_2$	100	100	100	69
$UO_2(NO_3)_2$	100	95	85	
$Bi(NO_3)_2 \cdot 5H_2O$	100	100	0	
$AuCl_3 \cdot 2H_2O$	100	100	0	
$Cd(NO_3)_2$	100	98	0	
$PdCl_2 \cdot 2H_2O$	100	95		
$CuSO_4$	100	74		
$Pb(NO_3)_2$	97			

* Concentration given as that when mixed with an equal volume of virus.

† The actual molar concentration is one-half the listed value. Other compounds had low antiviral activity and were of doubtful significance for this concentration. They are listed as follows: molybdate 90%, indium nitrate 89%, antimonyl potassium tartrate 82%, cobalt (ous) nitrate 82%, ferric chloride 76%, chromium (ic) nitrate 74%, stannic chloride 68%, manganous chloride 64%, platinum (ic) chloride 55% and lanthanum chloride 38%.

inactivate totally the virus inoculum. Five other cations, Uranyl: UO_2^{++}, Bismuth: Bi^{++}, Gold: Au^{+++}, Cadmium: Cd^{++}, and Palladium: Pd^{++}, showed significant activity at 10^{-4}M while the two others, Copper: Cu^{++} and Lead: Pb^{++} were active at 10^{-3}M. Agents with some activity at 10^{-3}M are listed in the footnote and include: ammonium molybdate, In^{+++}, SbO^{+}, Co^{++}, Fe^{+++}, Cr^{+++}, Sn^{++++}, Mn^{++}, Pt^{++++} and La^{+++}. Other metallic ions of both high and low molecular weight which were included in this survey gave little or no evidence of antiviral properties at concentrations of 10^{-3}M or less. These included: Li^{+}, Na^{+}, Mg^{++}, Al^{+++}, K^{+}, Ca^{++}, VO^{++}, Fe^{++}, Ni^{++}, Zn^{++}, Ge^{++++}, Rb^{+}, Sr^{++}, Ru^{+++}, Rh^{+++}, Cs^{+}, Ba^{++}, and Tl^{+}. These compounds were mainly salts of nitrate or chloride but also included was an occasional iodide, oxide (as for germanium), hydroxide (as for lithium), and sulfate. Most of these compounds at 10^{-1} to 10^{-2}M, with the buffering system used, had a pH of 4.0 or less and any antiviral effect at this level could be attributed to the hydrogen ion concentration rather than to the cation. The results shown, therefore, do not include antiviral activities below 10^{-3}M.

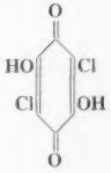
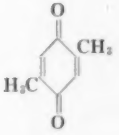
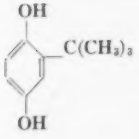
Table 2 provides the most interesting information in this survey. It will be noticed that many of the listed compounds are derivatives of p-benzoquinone (quinone) which heads the list. The extremely high antiviral activity of this compound is better appreciated when one again considers that a 10^{-5}M solution amounts to approximately 1.0 μg/ml., a figure which unquestionably is equal to the activity of some of the best antibacterial antibiotics. A comparable activity to that of quinone was exhibited by 2, 3, 5, 6 tetrachloro-p-quinone (chloranil) and to a lesser degree by hydroquinone.

A fairly high activity was demonstrated by chloranilic acid. This compound was completely active at 10^{-3}M, 90-percent active at 10^{-4}M and 70-percent active at 10^{-5}M. Why certain agents tend to have this spread of activity or slowly decreasing activity over 10-fold decreases in concentration is not known. One explanation might be that such a compound is quite active but is slower acting and needs a longer incubation period for the reaction to go to completion. Dimethylbenzoquinone possessed somewhat less antiviral activity than quinone.

Hydroquinone, a strong reducing agent which is easily oxidized in the air to quinone, was tested for its virus inactivating property under both aerobic and anaerobic conditions.

TABLE 2

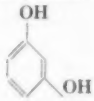
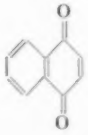
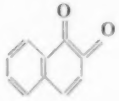
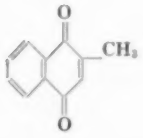
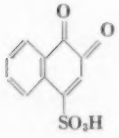
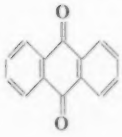
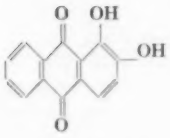
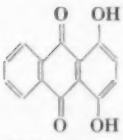
VIRUS INACTIVATION BY QUINONE DERIVATIVES AND SOME SUPPLEMENTARY COMPOUNDS

	Percent Virus Inoculum Inactivated					
	Concentration* of Chemical Agent (molarity)					Formulae
	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	
Benzoquinone (quinone)		100	100	100	0	
Chloranil		100	100	100	52	
Chloranilic acid		100	87	70		
2,5-dimethylbenzoquinone			100	91	0	
Hydroquinone	100	100	100	99	0	
Hydroquinone under anaerobic conditions	100	100	99	0		
Tertiary butyl hydroquinone		100	96	0		
Catechol	95	80	51	0		

(*Continued on following page*)

* Concentration given as that when mixed with an equal volume of virus. The actual molar concentration is one-half the listed value.

TABLE 2—(*Continued*)

	Percent Virus Inoculum Inactivated					Formulae
	Concentration* of Chemical Agent (molarity)					
	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	
Resorcinol	79	0	0	0		
1,4-naphthoquinone	100	100	100	98	78	
1,2-naphthoquinone		100	100	97	68	
Menadione		97	58	0		
1,2-naphthoquinone, 4-sulfonic acid	100	98	0			
Anthraquinone		100	74	61		
Alizarin		99	51			
Quinizarin			99	83	40	

(*Continued on following page*)

TABLE 2—(*Continued*)

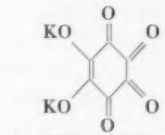
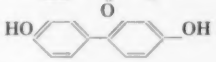
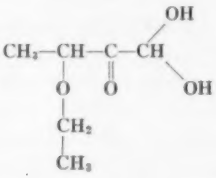
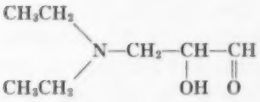
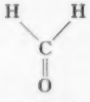
	Percent Virus Inoculum Inactivated					Formulae
	Concentration* of Chemical Agent (molarity)					
	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	
Rhodizonic acid potassium salt	99	0	0			
p,p′biphenol		88				
Kethoxal	100	100	0			
3-diethylaminolactaldehyde	91	0				
Formaldehyde	100	79	0			

TABLE 3

VIRUS INACTIVATION BY MISCELLANEOUS COMPOUNDS

Chemical Agent	Percent Virus Inoculum Inactivated			
	Concentration* of Chemical Agent (molarity)			
	10^{-2}	10^{-3}	10^{-4}	10^{-5}
Sodium desoxycholate	100	100	99	0
Prednisolone	100	0		
4,5-diiodofluorescein		100	100	65
p-chloromercurisodium benzoate	100	100	100	
Cyproheptadine†		100	0	
Benzimidazole	89	63		
2-methyl benzimidazole	100	0		
Phenol	82	57		
$KMnO_4$	100	98	90	56
Iodine (as I_2 in KI^2)	100	100	0	
KIO_2	100	0		
Ascorbic acid	100	90		

* Concentration given as that when mixed with an equal volume of virus. The actual molar concentration is one-half the listed value.

† Potassium iodide not antiviral at 1%.

The latter was done by manipulating virus transfer to the chemical agent by the use of Warburg flasks in an anaerobic (hydrogen) jar. Thus one fluid could be mixed with another by tilting the jar after all traces of oxygen had been removed from the fluids and the surrounding atmosphere. Under these conditions the antiviral activity of hydroquinone was recorded at a 10-fold lower concentration (10^{-4}M). Opportunity still existed for this agent to be oxidized during the brief interval when the anaerobic jar was opened and the fluids were inoculated onto the chorioallantoic membrane surfaces and also during the ensuing incubation of the eggs before the virus—if still active—could infect cell foci. The butyl derivative of hydroquinone exhibited about the same activity as anaerobic hydroquinone.

The isomers of hydroquinone, for example, o-dihydroxyquinone (catechol) and m-dihydroxyquinone (resorcinol) were much less active than the parent compound and their highest virus inactivating values were, respectively, 95 percent and 79 percent at 10^{-2}M.

Single and multiring analogues of quinone were found to have a variety of activities; 1,4-naphthoquinone and 1,2-naphthoquinone were approximately as active virus neutralizing agents as quinone and chloranil, that is, a 10^{-5}M concentration caused 98 and 97 percent virus inactivation; 2-methyl-1,4-naphthoquinone (menadione) which differed from 1,4-naphthoquinone only in its 2-methyl grouping gave a much lower activity: 97 percent and 58 percent at 10^{-3}M and 10^{-4}M respectively. Likewise, the 4-sulfonic acid derivative of 1,2-naphthoquinone was 98 percent effective only at 10^{-3}M. Anthraquinone was 100 percent active at 10^{-3}M but was still active at 10^{-5}M. Alizarin was 99 percent active at 10^{-3}M, quinizarin was 99 percent active at 10^{-4}M and thereupon decreased slowly to 40 percent at 10^{-6}M. Vitamin K (not listed) was only 70 percent active at 10^{-3}M and is, therefore, significantly lower in activity than its synthetic analogue, menadione.

Other compounds represented in Table 2 are not derivatives of quinone but are included for comparison for special reasons. Rhodizonic acid, for instance, was introduced because of its strong structural resemblance to quinone, that is, it possesses two carbonyl groups oriented para to each other with one alternating double bond. This agent was a comparatively weak antiviral agent. P,p′-biphenol possesses two hydroxyl radicals in para position but separated from each other by the two benzene rings. The compound was tested to see if the more distantly located para hydroxyl radicals would exhibit the same reactivity as hydroquinone but it showed only 88 percent inactivation at 10^{-3}M.

Kethoxal* (β-ethoxy-α-ketobutyraldehyde hydrate) and lactaldehyde 3-diethylamino-HCl (U-1671)* are related compounds that are antiviral for Newcastle disease and other viruses.[8] These compounds were tested for comparative purposes; the highest activity reached was that of Kethoxal (100 percent at 10^{-3}M) while U-1671 was much lower in activity (91 percent at 10^{-2}M).

Formaldehyde which is employed universally for virus inactivation for producing vaccines was also tested and was found to be 100 percent active at 10^{-2}M and 79 percent at 10^{-3}M.

In Table 3 are found a miscellany of agents, some related some unrelated. The first, sodium desoxycholate, represents those compounds with strong surface active properties which are known to be highly antiviral for a variety of viruses.[9,10] Others were tried, for example, sodium lauryl sulfate, Zephiran and Wescodyne, and all tended to fall within the same range of activity by the method used. Desoxycholic acid, which is poor in surface activity and the free acid of

* Kindly supplied by the Upjohn Company, Kalamazoo, Michigan.

the former compound, is noted to have very weak antiviral activity. Prednisolone, one of the steroids noted for its serious contraindications in acute herpetic infections, is noticed to have a small degree of antivirus activity on the free virus (100 percent inactivation at 10^{-2}M); 4,5-dio-odofluorescein is the only other organic compound tested that was highly active (100 percent at 10^{-4}M). One exception, an organic compound No. 8318 kindly supplied by Smith, Kline and French laboratories, was also 100 percent active at 10^{-4}M. The formula has been withheld. In comparison with the diiodo derivative, ordinary fluorescein (not listed) was active at 10^{-1}M but not much below 6×10^{-2}M. The latter concentration (about two percent) is that generally used in practice for staining dendritic ulcers.

A highly toxic compound, p-chloromercurisodium benzoate, was strongly active (100 percent at 10^{-4}M) and undoubtedly is related to the presence of mercury. Cyproheptadine, a new antiserotonin and antihistaminic from Merck, Sharp and Dohme, was 100 percent at 10^{-3}M. The benzimidazole derivatives are two of many similar compounds which inhibit the development of influenza virus in eggs.[11] They are shown to have little direct activity against herpes virus. Phenol was also of low activity.

The antiviral activity of some inorganic oxidizing agents is also shown. Potassium permanganate was 98 percent active at 10^{-3}M dropping off to 90 percent at 10^{-4}M. Iodine was 100 percent active at 10^{-3}M and potassium iodate was the same at 10^{-2}M. As a reducing agent ascorbic acid was less than fully active against the virus at 10^{-3}M.

The greater proportion of compounds tested against herpes virus possessed no significant antiviral activity as far as a direct interaction with extracellular virus was concerned. These compounds are listed below. Most of them had no activity at 10^{-2} and 10^{-3}M and only a few had slight activity at 10^{-3}M. Some were even inactive at 10^{-1}M.

ACIDS*

Acetic
Ethoxyacetic
Propanoic
Butyric
Hexanoic
Decanoic
Iodoacetic
β iodopropanoic
β chloropropanoic
Pyruvic
Succinic
Mercaptosuccinic
Versene
Tannic
Periodic
Folic
Kojic

AROMATIC COMPOUNDS

Salicylic acid
5 nitrosalicylic acid
Sulfanilic acid
Nitrosalicylaldehyde
2,4-dinitrophenol
Phloroglucinol
O-iodophenol

ALICYCLIC COMPOUNDS

Cyclohexane
Cyclohexanecarboxylic acid
Cyclohexanepropionic acid
Cyclohexylamine
Cyclohexanol
Cyclohexyl acetate
Cyclohexanone
1,2-cyclohexanedicarboxylic anhydride
Inositol

MISCELLANEOUS COMPOUNDS

Potassium cyanide
Sodium nitrite
Sodium acetate
Hydroxylamine
Urea
Choline
Trimethylolnitromethane
Tetra-n-butylammonium bromide
Cysteine
Citrus bioflavonoid compound (CVP)†
Ether
Allyl ethyl ether
Ethylene oxide
Propylene oxide
Allylformate
1,2-propanediol
Ethanol
Acetone

HETEROCYCLIC COMPOUNDS

Caffeine
Barbituric acid
Allantoin
Hydantoin
Alloxan
6-mercaptopurine
6-nitroquinoline
Coumarin
3-hydroxyflavone
Furildioxime
2-furaldoxime
5-nitro-2-furanmethanedioldiacetate
Nitrofuran
Santonin
2-pyridine aldoxime methiodide

THERAPEUTIC TRIALS IN THE RABBIT

The most promising chemical agents as determined by their ability to inactivate virus in vitro were tested for similar activity in preventing the formation of dendritic ulcers in the rabbit cornea. Some compounds with little or no in vitro activity were also in-

* The hydrogen ion rapidly inactivated herpes simplex at low pH. At pH values above 4.5 or 5.0 it rapidly lost its effect. The above acids were so buffered that the pH was greater than 5.0 at 10^{-2}M acid.

† Kindly supplied by the U. S. Vitamin and Pharmaceutical Corp., New York.

cluded for in vivo trial. Therapy was applied only one hour postinoculation as already described. The number of animals tested in each instance varied considerably and was as low as one or two animals in a number of cases. Extensive tests were conducted for some of the more potent agents, however, and included 28 rabbits for silver nitrate and 14 rabbits for sodium desoxycholate. Toxicity tests were usually made on animals that had been used for other experiments and would otherwise be rejected. Toxic effects were demonstrated mainly by corneal staining with one-percent methylene blue and fluorescein which revealed epithelial damage. Conjunctivitis and chemosis also served as criteria.

Greatest emphasis was placed on the most active cations, quinones and surface active compounds. Sodium desoxycholate was of no benefit in treating herpetic keratitis and was toxic at concentrations above 0.05 percent. It was nevertheless used as an eyewash at 0.01 and 0.02 percent in a number of tests where 0.005 M to 0.01 M (0.17 percent) silver nitrate was applied. In one such trial a decrease in the amount of dendritic figures was noted in 10 out of 21 eyes but no total preventive effect could be achieved. These results are not to be taken as evidence of an active in vivo action by the reagents used. Dendritic patterns in the treated eyes, though diminished in intensity, lasted as long as those of control eyes. Whatever beneficial action may have occurred it is believed that it was by way of inactivation of liberated "free" virus thereby minimizing the amount of virus available for infecting new cells. Toxic effects to the cornea by $AgNO_3$ occurred at 0.05 M (0.85 percent) but not at 0.01 M (0.17 percent). Cauterization of a dendritic ulcer with a single application of 0.5 percent $AgNO_3$ was well tolerated and corneas so treated returned to normal clarity. A precipitate of AgCl was also tried in the hope that the solid would maintain a prolonged supply of silver ions but the substance was toxic if applied every five minutes. It was safe if applied hourly but gave results that were equivocal.

Quinone, which is highly toxic for the cornea and other tissues could be applied safely only at 10^{-4}M at five-minute intervals or at 10^{-3}M at hourly intervals. Under these schedules, however, no satisfactory effect was noted in corneal infections. Three derivatives of quinone: chloranil, alizarin and quinizarin were found to be well tolerated by the rabbit cornea even when applied as the dry powder. The cornea remained clear, intact and without inflammation. These were therefore applied as the dry powder one hour after inoculation and three to four times each day thereafter. The results were in favor of the latter two compounds with the same type of mild benefit as already mentioned but without true significance. Other quinone derivatives tested: 1,2-; 1,4-; and 2 methyl-1,4-naphthaquinone, were highly toxic at 0.001 M and therefore valueless.

A few of the active agents were applied to infected rabbit corneas by iontophoresis for limited periods (two minutes at 1.6-2.0 milliamperes). Under these conditions minimal damage occurred to the cornea but the treatment offered no advantage over simple topical application of these agents.

All other compounds that were similarly tested and found to cause no alteration in the severity and duration of herpetic keratitis are listed at bottom of next page.

Attempts at reactivation of virus

An experiment was run to see if the process of virus inactivation by two of the highly active chemicals, quinone and silver nitrate, could be reversed by dilution. The chemical agents at 10^{-3}M concentration were each mixed with an equal volume of a virus inoculum containing over 10^7 pock-forming units/ml. and incubated one hr. at 36°C. The mixtures were then diluted in BGL by 10^{-3} and 10^{-4} and reincubated for one more hour at which time aliquots of 0.1 ml. were inoculated on groups of four eggs each. No virus

was demonstrable in the diluted mixtures even though the controls showed that they normally would have had 1,100 and 110 pock-forming units respectively. In the former instance the quinone and silver nitrate had a final concentration of 10^{-6}M and in the latter mixture it was 10^{-7}M, both concentrations being below the active range of antiviral activity.

In another experiment with quinone the extent of its range of virus inactivation against large inocula was measured. It was found that when 10^{-4}M quinone was incubated for one hour with undiluted virus (that is, 2×10^7 pock-forming units/ml.) a fraction of 2.16×10^{-4} or 0.02 percent of virus survived. Since quinone may react with protein it is probable that a fraction of it also interacted with extraneous chorioallantoic-membrane proteins in the crude virus suspension.

Discussion

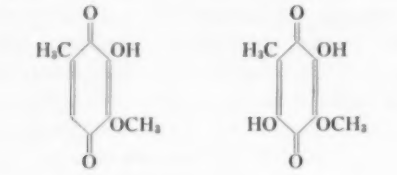
It is apparent from the preceding data that many agents exist which have potent antiviral properties against extracellular herpes-simplex virus. The mechanism by which this virus-inactivating action occurs is presently unknown and possibly more than one mode of action is involved depending on the type of chemical agent employed. Surface-active compounds like sodium desoxycholate have a type of action on the virus that is probably quite different from that of the silver ion and quinone. It is possible that these two latter agents also differ from each other in their mode of antiviral activity. One detergent, sodium lauryl sulfate, has been used to separate the nucleic acid portion of tobacco mosaic virus from its external protein shell[12] and this type of action was probably involved in the detergent inactivation of herpes simplex. For the present it appears that the action of quinone and silver nitrate against the virus is irreversible. High dilutions of proper virus-quinone and virus-silver nitrate mixtures did not lead to reactivation of the virus.

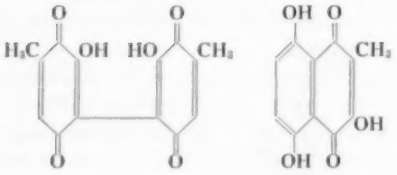
The exceptional antiviral activity of quinone and some of the quinone derivatives tested in this study should provide a rich source of chemical compounds for further investigation. A considerable number of such compounds exist and many are obtained from biologic sources including bacteria, fungi, higher plants insects and mammals.[13–15] Included among the host of naturally occurring quinone derivatives are many which especially lend themselves for future study: quinones such as fumigatin (I), a product of Aspergillus fumigatus Fresnius,[16] spinulosin (II), from the same source and from Penicillium spinulosum Thom;[16–18] phoenicin (III), from P. phoeniceum van Beyma;[19] and hydroxydroserone (IV) from the bulbous root growths of Drosera whit-

P-chloromercurisodiumbenzoate (0.01%)
Mercuric chloride (0.1, 0.1%)
Bismuth nitrate (0.001 M)
Palladium chloride (0.001 M)
Vitamin K_1 oil
4',5'-diiodofluorescein (0.005 M)
S.K.F. No. 8318* (0.04 M)
Cyproheptadine† (0.001 M)
Potassium permanganate (0.1%)
Ascorbic acid (1.0%)
Sodium lauryl sulfate (1.0%)
Zephiran chloride (0.1%)
Wescodyne‡ (0.01%)
Choline (0.1%)
Iodopropionic acid (1.0%)
Succinic acid (0.5%)
Mercaptosuccinic acid (0.5, 0.1%)
Versene (2.0, 0.8, 0.2%)
Cyclohexanepropionic acid (0.1, 0.01%)
5-nitro-2 dimethoxyfurane diacetate (0.01 M)
Citrus bioflavonoid compound (0.1, 0.2%)
Iodine (cauterization, 2% in KI)
Ether (cauterization, 100%)

* Kindly supplied by Smith, Kline & French Laboratories, Philadelphia.
† Kindly supplied by Merck, Sharp & Dohme, West Point, Pennsylvania.
‡ West Disinfecting Co., New York.

takeri[30] are only a few examples that are worthy of study and which will be investigated in this laboratory as soon as samples are available.





Evidence of naturally occurring antiviral substances is beginning to be reported in the literature. Examples are Ehrlichin, an antibiotic produced by Streptomyces lavendulae,[21] myxoviromycin from Streptomyces sp.,[22] and an unnamed agent from Penicillium funiculosum.[23]

These agents all possess qualities comparable to true antibacterial antibiotics in that they are naturally derived (especially from fungal sources) and that they inactivate viral species in extremely low concentrations (in the order of a few μg./ml.). A primary difference from other antibiotics is that they are antiviral for certain viruses. Perhaps a special term "antivirotic" could be designated for such agents. This would provide a distinction between antibiotic substances which act against widely different types of micro-organisms: for example, those which act against bacteria, fungi, rickettsiae and the atypical viruses, the chlamydozoaceae, by an interference with an inherent metabolic process of the micro-organism, and those, which act by an unknown mechanism against viruses which have no known intrinsic metabolism. In the case of natural quinone derivatives it is expected that some of these will prove to be as potent antiviral agents as some of the synthetic ones tested.

Three earlier references of an antiviral action by benzoquinone were found following the present study.

Thompson[24] had demonstrated inhibition of vaccinia virus multiplication in tissue cultures containing benzoquinone or hydroquinone. A decrease in virus titers occurred to the extent of a log -1.00 to -2.00 at 10^{-5} to 10^{-3}M benzoquinone; some evidence of a direct action of the chemicals on the virus in vitro was also suggested.

Burney and Golub[25] reported similar evidence for hydroquinone against psittacosis virus. The mode of action in both instances was considered to be due to tissue enzyme inhibition by these compounds.

Hollinshead and Smith[26] reported on the effectiveness of a number of quinone and hydroquinone derivatives for inhibiting cytopathogenic effects in tissue cultures by poliomyelitis virus. The chemicals were added to the cell cultures 24 hours after virus inoculation. The hydroquinones possessed the greatest activity (approximately 2.0 to 30 μg./ml.), whereas, quinone and its derivatives were considerably lower in antiviral activity (approx. 60 to 500 μg./ml.). Further studies with the natural derivatives of benzonaphtho- and anthra-quinone on different viruses for direct and indirect antiviral action should be undertaken to see if this group of compounds could properly be classified as antiviral or "antivirotic" in nature.

In the in vivo tests on the rabbit cornea with an agent as highly active as quinone it was shown that a 10^{-4}M concentration was well tolerated when applied topically at five-minute intervals as was a 10^{-3}M concentration when applied at 60-minute intervals. Although these dosages were respectively 10 and 100 times greater than the total virus-inactivating end-point, they did not prevent the development of herpetic keratitis even when applied only one hour after virus inoculation. This result may be attributed

either to a failure for this small molecule to penetrate infected cells, or to a chemical neutralization of quinone by the host cell walls or cell contents. A similar consideration may be applied to the action of the silver ion which is approximately as active as quinone.

The importance of the spatial relation of functional groups in isomeric compounds is evident in the decreasing order of activity in the compounds: Hydroquinone, o-dihydroxyquinone; these agents showed roughly a comparative activity at concentrations of 10^{-4}, 10^{-3} and 10^{-2}M respectively. Large reduction in activity occurs also according to the type and location of functional groups in active compounds like benzoquinone and naphthoquinone. This is made evident in the great decrease in activity by adding a *4-sulfonic* or *2-methyl* grouping to naphthoquinone. In the anthraquinones there was also less activity for a substance like alizarin, with hydroxyl groups in positions *1* and *2*, but relatively undiminished antiviral action in its quinizarin isomer where the two hydroxyl groups were located at positions *1* and *4* or para to each other.

The significance of all these differences is not fully clear and many more related compounds must be tested in order to obtain a proper perspective of any basic pattern of activity. Because the quinones are strong oxidizing agents the question of the level of their individual E_h potentials must be considered. The high level of these values is probably important but not absolute. In the case of benzoquinone, 1,2 naphthoquinone and 1,4 naphthoquinone the E_h potential in decreasing order is: 0.699, 0.555 and 0.470 yet the latter two compounds with lower potentials were somewhat more active than benzoquinone.

An interesting feature of virus inactivation by cationic agents is the relatively close relationship that the most active ones exhibited in the periodic table of elements. This group, so to speak, comprised those metals which gave 95 to 100 percent virus inactivation at a concentration of 10^{-4}M or less. Two of these (Ag^{+} and Hg^{++}) were 100 percent active at 10^{-5}M. In considering the position of these elements in the accompanying periodic table, five of the most active ones are found to be located in one small area. These are designated by the symbols printed in bold face type and are palladium (Pd), silver (Ag), cadium (Cd), gold (Au) and mercury (Hg). The other highly active elements bismuth (Bi) and uranium (U) occur in groups more distant from group IB and IIB which contain Ag and Hg the two most active elements. Uranium which was active as the uranyl complex $(UO_2)^{++}$ is not listed in the table but occurs in the actinide series of elements. This element occurs in group IIIB in the table as does lanthanum (La) and both are the only representatives tested in either of the two special series of ele-

PERIODIC TABLE OF ELEMENTS

IA	IIA	IIIB	IVB	VB	VIB	VIIB		VIIIB		IB	IIB	IIIA	IVA	VA	VIA	VIIA	Inert Gases
H																	
*Li**	Be											B	C	N	O	F	Ne
Na	*Mg*											*Al*	Si	P	S	Cl	A
K	*Ca*	Sc	Ti	*V*	*Cr*	*Mn*	*Fe*	*Co*	*Ni*	*Cu*	*Zn*	Ga	*Ge*	As	Se	Br	Kr
Rb	*Sr*	Y	Zr	Nb	*Mo*	Tc	*Ru*	*Rh*	**Pd**	**Ag**	**Cd**	*In*	*Sn*	*Sb*	Te	*I*	Xe
Cs	*Ba*	*La*†	Hf	Ta	W	Re	Os	Ir	*Pt*	**Au**	**Hg**	*Tl*	*Pb*	*Bi*	Po	At	Rn
Fr	Ra	Ac‡															

* Italic elements are the ones tested in this study.
† The lanthanide series is not listed but represented by lanthanum (La).
‡ The actinide series is not listed but represented by Actinium (Ac); uranium as the uranyl ion (UO_2^{++}) is the only member tested.

ments. The latter had a very small degree of activity at 10^{-3}M. Copper (Cu) occurring in the same group as silver was a fairly active cation. Although all of the elements have not been tested the data indicate that strong antiherpes activity is not necessarily a function of molecular weight and that individual chemical properties are more important in this respect. Further studies along this line with other viruses should be attempted.

In conclusion it might be claimed that there are a number of highly active antiviral agents against herpes-simplex virus. They include wetting agents of various types, certain cations and quinone analogues. Undoubtedly other types exist. No agent among these was revealed to be effective therapeutically for local application on surface (corneal) infections. However, it might be recommended that a few be employed at nontoxic dosages for clinical trial and evaluation. Specifically silver nitrate might be recommended (especially since it is used transiently in infants for prophylaxis against ocular neonatorum at one-percent) at safe concentrations. A concentration of 0.5 percent in a single application as a chemical cautery has been found to be tolerated in several patients with dendritic corneal ulcers. In comparison with iodine, which has been in use as a cautery agent since it was introduced by Gundersen in 1936,[27] silver nitrate would appear to be upward of 100 times as potent a virus inactivating chemical. Silver nitrate, therefore, could be used at much lower concentrations than iodine (which is currently employed at concentrations between two and seven percent). The use of much lower concentrations of chemical cautery agents should be an advantage in obviating much of the tissue irritation that occurs from this form of therapy.

Summary

1. A number of chemical compounds in low concentration have been found capable of inactivating herpes simplex virus in vitro.

2. Compounds with the most potent activity were certain derivatives of quinone and a small group of metallic cations that occur in a fairly well-circumscribed area of the periodic table of elements.

3. The greatest range of antiviral activity amounted to a total inactivation of a given virus inoculum by a concentration of the chemical agent as low as 10^{-5}M.

4. In spite of impressive virus neutralizing properties of some agents, and of low tissue toxicity in certain of these, no significant degree of antivirus activity could be obtained in treatment of corneal infections in the rabbit.

5. The significance of these results is discussed and suggestions are made for a substitute chemical cautery in treating human dendritic ulcers of the cornea.

1601 Spring Garden Street (30).

References

1. Hurst, E. F., and Hull, R.: The chemotherapy of virus diseases, with brief consideration of the influence of dietary, hormonal and other factors in virus infections. Pharmacol. Rev., **8**:199-263, 1957.

2. Horsfall, F. L., and Tamm, I.: Chemotherapy of viral and rickettsial diseases: Annual Review of Microbiology **11**. Annual Reviews Inc., Palo Alto, Calif., 1957, pp. 339-370.

3. Burnet, F. M., and Lush, D.: Inactivation of herpes virus by immune sera: Experiments using the chorioallantoic membrane technique. J. Path. & Bact., **48**:275-286, 1939.

4. Sery, T. W.: Random occurrence of herpetic disciform keratitis in rabbits. Am. J. Ophth., **48**:57-71, 1959.

5. Amos, H.: The inactivation of herpes simplex by phosphatase enzymes. J. Exper. Med., **98**:365, 1953.

6. Hallett, J. W., Leopold, I. H., Vogel, A. W., Cannon, E. J., and Steinmetz, C. G.: Treatment of experimental herpes simplex keratitis in the rabbit. AMA Arch. Ophth., **46**:33, 1951.

7. Hallett, J. W., Naib, K., and Leopold, I. H.: Control of experimental herpes simplex virus keratitis. AMA Arch. Ophth., **54**:573-579, 1955.

8. McLimans, W. F., Underwood, G. E., Slater, E. A., Davis, E. V., and Siem, R. A.: Antiviral activity of dicarbonyls and related compounds in embryonated eggs. J. Immunol., **78**:104-111, 1957.

9. Burnet, F. M., and Lush, D.: The action of certain surface-active agents on viruses. Australian J. Exper. Biol. & Med. Sc., **18**:141, 1940.

10. Theiler, M.: Action of sodium desoxycholate on arthropod-borne viruses. Proc. Soc. Exper. Biol. & Med., **96**:380-382, 1957.

11. Tamm, I., Folkers, K., Shunk, C. H., Heyl, D., and Horsfall, F. L., Jr.: Inhibition of influenza virus multiplication by alkyl derivatives of benzimidazole: III. Relationship between inhibitory activity and chemical structure. J. Exper. Med., **98**:245-259, 1953.

12. Fraenkel-Conrat, H., and Williams, R. C.: Reconstruction of active tobacco mosaic virus from its inactive protein and nucleic acid components. Proc. Natl. Acad. Sc. (U.S.), **41**:690-698, 1955.

13. Fieser, L. F., and Fieser, M. Organic Chemistry. Boston, Heath, 1950.

14. Thomson, R. H.: Colloquium on naturally occurring quinones and their biological roles: Introduction: Distribution and nature of the naturally occurring quinones. Biochem. J., **73**:(No. 1, Proc. Biochem. Soc. IP) 1959.

15. Green, D. E., and Lester, R. L.: Role of lipides in the mitochondrial electron transport system. Fed. Proc., **18**:987-1000, 1959.

16. Anslow, W. K., and Raistrick, H.: XCI. Studies in the biochemistry of microorganisms. LVII. Fumigation (3-hydroxy-4-methoxy-2:5-toluquinone) and spinulosin (3:6 dihydroxy-4-methoxy-2:5-toluquinone) metabolic products respectively of Aspergillus fumigatus Fresnius and Penicillium spinulosum Thom. Biochem. J., **32**:687-696, 1938.

17. Anslow, W. K., and Raistrick, H.: CCXCII. Studies in the biochemistry of microorganisms. LIX. Spinulosin (3:6-dihydroxy-4-methoxy-2:5-toluquinone) a metabolic product of a strain of Aspergillus fumigatus Fresnius. Biochem. J., **32**:2288, 1938.

18. Raistrick, H.: The production of quinones by "moulds." Synthesis of spinulosin (3,6-dihydroxy-4-methoxy-2,5-toluquinone). Chem. & Indust., **16**:293-294, 1938.

19. Friedheim, E. A. H.: The biochemistry of the lower fungi: I. Isolation of the red pigment of Penicillium phoenicium, phenicin. Helv. Chim. Acta, **21**:1464-1465, 1938.

20. MacBeth, A. K.: The chemistry of the hydroxynaphthaquinones and of the coloring matters of Drosera whittakeri. Australian Chem. Inst. J. & Proc., **4**:207-222.

21. Groupe, V., Frankel, J. A., Lechevalier, M. P., and Waksman, S. A.: Antiviral properties of Ehrlichin, an antibiotic produced by Streptomyces lavendulae. J. Immunol., **67**:471, 1955.

22. Kobayashi, N.: Studies on antiviral antibiotics from streptomyces: XII. Further studies on the antiviral antibiotic myxoviromycin. Tohoku J. Exper. Med., **70**:95-102, 1959.

23. Shope, R. E.: An antiviral substance from Penicillium funiculosum: I. Effect upon infection in mice with swine influenza virus and Columbia SK encephalomyelitis virus. J. Exper. Med., **97**:601-625, 1953.

24. Thompson, R. L.: The effect of metabolites, metabolite antagonists and enzyme-inhibitors on the growth of the vaccinia virus in maitland type of tissue cultures. J. Immunol., **55**:345-352, 1948.

25. Burney, T. E., and Golub, O. J.: The effect of certain enzyme inhibitors on the activity and growth of psittacosis virus. J. Immunol., **60**:213-221, 1948.

26. Hollinshead, A. C., and Smith, P. K.: Relative effectiveness of certain inhibitory chemicals on the three types of poliomyelitis virus. J. Pharmacol. & Exper. Therapeut., **117**:99-100, 1956.

27. Gundersen, T.: Herpes corneae with special reference to its treatment with strong solution of iodine. Arch. Ophth., **15**:225, 1936.

AN EVALUATION OF HEPARIN IN THE TREATMENT OF SENILE MACULAR DEGENERATION*

NORMAN F. SCHWILK, JR., M.D., AND ALAN J. ROSENBERG, M.D.
San Francisco, California

For several years the treatment of senile macular degeneration with aqueous heparin has been in vogue. In 1943 it was shown experimentally by Hahn[1] that heparin has the ability to reduce plasma turbidity by converting large, abnormal lipoprotein molecules into smaller, more nearly normal-sized molecules and that the effect lasts several

* From the Department of Ophthalmology, University of California School of Medicine.

Fundus photographs were taken by Dr. Stacey Mettier, Jr., through the courtesy of the Cardiovascular Research Institute, University of California School of Medicine. The heparin used in this study was donated in part by Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

days, diminishing gradually. On the basis of this experimental work the intermittent administration of heparin has been used in the treatment of various clinical conditions stemming from arteriosclerosis (Kory,[2] Orna,[3] Brown,[4] Engelberg[5,6]).

In a discussion of the heparin treatment of diabetic retinopathy, Berlin[7] stated (1954) that Vannus had treated a small series of five cases of arteriosclerotic retinopathy with heparin, 50 to 100 mg. per day for one or two weeks, and that he had reported some improvement in two cases and considerable improvement in a third, but no convincing results. In 1957 Mylius and Stark[8] reported that 11 cases of arteriosclerotic macular disease were improved by daily injections of 100 mg. of heparin but they gave no details.

In 1958 Keeney and Jain[9] published an excellent discussion of the treatment of senile macular degeneration by lipotropic substances, vitamin K and heparin. Eleven cases were treated by 100 mg. of aqueous heparin intravenously, twice a week for four weeks. Two cases showed distinct improvement, one definitely worsened, and eight remained unchanged. In his discussion of this paper, Newell[10] mentioned treating 10 other such cases, some with heparin and some with a placebo, with no improvement in any patient receiving the heparin.

Over the past six years, Harrington[11] has treated approximately 100 of these cases with heparin administered intramuscularly or subcutaneously. Some of his cases have improved spectacularly, others not at all. He has refrained from publishing a report of this series because of the difficulty of evaluating this kind of therapy.

Rome[12] reported the results of treating a series of 23 cases of disciform macular degeneration and senile macular degeneration with twice weekly intravenous injections of heparin sodium, 100 mg. There was marked subjective and objective improvement in half the cases with disciform macular degeneration, and favorable results also in a little less than half of the smaller group of cases of more typical arteriosclerotic senile macular degeneration. In this series no controls were included.

Recently Havener, et al.,[13] and Bierman[14] have treated similar series of patients with heparin and both have found its specific value highly questionable. These authors mentioned the slow, variable course of the disease and the fact that its psychic aspect is reflected in the patient's response to any intensive form of treatment.

Clinical study

In an attempt to evaluate the results of the use of heparin under controlled conditions, alternate patients of a selected series were given heparin sodium injections while the remaining patients received three-percent hypertonic saline solution, prepared so as to give the patient the same general sensation as from the injection of heparin. A total of 16 patients were subjected to the entire series of injections. Cases of disciform macular degeneration of the Kuhnt-Junius type were not included. Only patients with a visual acuity of 20/200 or better were accepted so that far-advanced, old, inactive cases were excluded. Among the 16 patients selected on this basis, there were seven in whom one eye had a visual acuity of less than 20/200. These seven eyes were eliminated from the experiment and each of the remaining 25 eyes, rather than each patient, was regarded as a separate experimental unit. The patients were not told that placebo medications were being used in some cases; they were told only that the medication being tested was of a new type which held some therapeutic promise.

The course of treatment consisted of twice-weekly intramuscular injections of heparin sodium, 100 mg., or of equal amounts of the placebo, for six months, immediately followed by a three months' course of twice-weekly intravenous injections of the drug or placebo in the same dosage. Bleeding times were not checked but no bleeding difficulties were encountered. One patient, not

included in the series, developed a mild generalized dermatitis shortly after the beginning of treatment which was then stopped; a causal relationship between the dermatitis and the heparin was never established.

The course of the disease was charted according to the patient's subjective impression of his visual efficiency, and according to measurements of visual acuity determined on a standard 20-foot lane. Visual fields were measured in only a minority of cases, since it was felt that if the treatment were to have practical value, it would have to improve vision enough to be recognized by the patient and to be measurable on the Snellen chart. For comparative purpose on an objective basis, photographs were taken at the beginning of the study, after six months, and after nine months.

A total of 13 eyes (in nine patients) were followed in the patients receiving the heparin solution. The visual acuity remained unchanged in 11 of these; in two it decreased markedly due to the development of the disciform type of macular hemorrhage.

A total of 12 eyes (in seven patients) were followed in the patients receiving the placebo solution; none of them showed a significant increase or decrease in visual acuity.

Almost without exception the patients in both groups reported definite subjective improvement in visual acuity at least some time during the course of treatment, and several expressed regret when the treatment was terminated.

Discussion

In a controlled study, 16 patients with senile macular degeneration were treated over a nine-month period with twice-weekly injections of heparin sodium or placebo. No improvement was observed. No valid conclusions could be drawn from so small a series, but the evidence strongly suggests that heparin is not specifically beneficial to the arteriosclerotic type of senile macular degeneration. The subjective improvement observed was in all probability related to the psychologic aspects of the disease; that is, the patient responded favorably to the frequent visits and examinations and to the opportunity afforded him to meet other patients with the same problems.

University of California
Medical Center (22).

References

1. Hahn, P.: (As quoted by Anfison, C., Boyle, E., and Brown, R.: Role of heparin in lipoprotein metabolism.) Science, **115**:583-586, 1952.
2. Kory R., Townes, A., Mabe, R., Dorris, E., and Meneely, G.: Drug evaluation in angina pectoris: khellin, heparin, peritrate. Am. Hearst J., **50**:308-321, 1955.
3. Orna, E.: Effect of heparin and placebo therapy on hypertension in geriatric patients. Ann. Med. Intern. Finniae, **44**:145, 1955.
4. Brown, K., and Rykert, H.: Heparin in the treatment of angina pectoris. Canadian M. A. J., **70**: 617-620, 1954.
5. Engelberg, H., Kuhn, R., and Steinman, M.: Controlled study of the effect of intermittent heparin therapy on the course of human coronary atherosclerosis. Circulation, **13**:489-498, 1956.
6. Engelberg, H., and Massell, T.: Heparin in the treatment of advanced peripheral atherosclerosis. Am. J. M. Sci., **225**:14-19, 1953.
7. Berlin, R.: Heparin treatment of diabetic retinopathy. Acta Ophth., **32**:711-716, 1954.
8. Mylius, K., and Stark, H.: The significance of arteriosclerosis in macular disease. Arch. f. Ophth., **156**:374-394, 1955.
9. Keeney, A., and Jain, M.: Macular disease of involutional type: classification and therapeutic approaches. Tr. Am. Ophth. Soc., **56**:247-262, 1958.
10. Newell, F. W.: In discussion of paper by Keeney and Jain.[9]
11. Harrington, D.: Personal communication.
12. Rome, S.: Heparin in senile macular degeneration. AMA Arch. Ophth., **57**:190-199, 1957.
13. Havener, W., Sheets, J., and Cook, M.: Evaluation of heparin therapy of senile macular degeneration. AMA Arch. Ophth., **61**:390-401, 1959.
14. Bierman, E.: Therapy of senile macular degeneration. Am. J. Ophth., **47**:405-407, 1959.

EPISCLERAL NODULES AND ERYTHEMA NODOSUM*

Report of a case with the pathologic findings

James L. McCarthy, M.D.
Oak Park, Illinois

Erythema nodosum is a reaction pattern of the skin in an inflammatory, symptomatic dermatitis often accompanied by constitutional symptoms and signs[1] but infrequently complicated by ocular pathologic conditions.

Preceding, during, or following a bout of erythema nodosum, ocular lesions have been observed, common among which are nodules of the sclera, episclera, and conjunctiva, uveitis, phlyctenular conjunctivitis, and episcleritis. Like the dermatologic component of this disease, scleral and conjunctival lesions usually are benign and have a self-limited course; however, loss of vision and, at times, the eye have occurred when the uveal tract becomes inflamed. A summary of ocular findings of reported cases collected from the literature is presented in Table 1.[2-41] The relative incidence of the various eye manifestations in erythema nodosum is listed in Table 2.

Erythema nodosum occurs most frequently between the first and third decades and during the spring and fall. The cutaneous lesions are characterized by oval or rounded painful nodules which develop rapidly—most commonly on the extensor surfaces of the arms or legs. These nodules do not ulcerate or suppurate but are tender when pressed. Tense, shiny, and bright red in color, the lesions frequently are raised above the surface of the adjoining skin. In a matter of weeks the skin lesions slowly disappear. Mucosal surfaces usually are not affected.[1, 42]

The reaction pattern of erythema nodosum can be evoked by bacterial, toxic, and chemical agents. Some of the most common are tubercle protein, nucleoprotein of hemolytic streptococci, and drugs (sulfonamides, antipyrenes, iodides, bromides). Characteristic

* From the Department of Ophthalmology, Cook County Hospital, Chicago, Illinois.

TABLE 1

Summary of previously reported cases of erythema nodosum with associated ocular lesions

Year	Author	Ocular Lesions	Remarks
1894	Beaudonnet[2]	Swollen red lesion of inner canthus. Changed to vesicle and left in 8 days	Possibly a case of erythema multiforme
1896	Brault[3]	Bilateral pterygia of a "knotty nature"	Skin lesions of the arms preceded ocular lesions which lasted one month
1899	Schneider[4]	Circumscribed episcleral nodules	
1901	Allan[5]	Bilateral iritis	Mild iritis appeared 2 weeks after onset of erythema nodosum
1902	Chaillous[6] (Case 1)	Bilateral conjunctival "papules" at internal angles	Patient also had erythema multiforme
1905	Shein[7]	Exudative conjunctivitis	Lesions thought to be embolic phenomenon
1905	Shein[7]	Conjunctival nodules	
1906	Reis[8]	Bilateral cyclitis and right hypopyon	Erythema nodosum thought to represent a primary lesion. Iritis became more intense with onset of erythema nodosum
1907	Burnand[9]	Iritis, keratitis, and episcleritis	Skin lesions appeared first. Patient also had erythema multiforme
1910	Lurie[10]	Bilateral plastic iritis	Suggested rheumatic etiology. Erythema nodosum followed the iritis
1912	Terson[11]	Erythema about pinguecu-lum	Suggested tuberculous etiology. Intraocular edema resulted in glaucoma
1914	Weil, et al.[13]	Nodules nasal conjunctiva	

TABLE 1 (*Continued*)

Year	Author	Ocular Lesions	Remarks
1914	Weil, et al.[1]	Edema of conjunctiva	
1914	Weil, et al.[12]	Bilateral nasal episcleral nodules	
1914	Weil, et al.[12]	Bilateral nasal episcleral nodules	
1916	Haab[13]	Herpes cornea febrilis, herpes zoster and nodules of conjunctiva	Suggested tuberculous etiology
1919	Gilbert[14]	Iridocyclitis with annular "knots" at root of iris. Recurrent hypopyon	Resultant vision affected eye less than 20/200
1923	Satanowsky[15]	Episcleritis	Etiology possibly tuberculosis, lues, or rheumatism
1925	Weltistscheff[16]	Conjunctival nodules	
1925	Kaznelson [7]	Recurrent iritis and hypopyon	Dermal and ocular lesions concurrent
1925	Cavara[18]	Recurrent uveitis	
1926	Fuchs[19]	Scleral nodules, iritis, and hypopyon	Patient had chronic subcutaneous and mucosal lesions
1928	Tow[20]	Bilateral phlyctenular conjunctivitis	Skin lesions appeared first. Rash of measles preceded erythema nodosum. Tuberculin skin test was four plus. Enlarged hilus glands on the chest film
1928	Rotth[21]	Bilateral nasal conjunctival nodules	Suggested tuberculous or rheumatic etiology
1928	Rotth[21]	Bilateral nasal conjunctival nodules	
1928	Josefsen and Malmgrem[22]	Conjunctival phlyctenules	Suggested toxic tuberculous etiology
1930	Rameev[23]	Conjunctival nodules	
1931	Shieck[24]	Conjunctival nodules	
1931	Krachmalnikov[25]	Conjunctival nodules and acute catarrhal conjunctivitis	Suggested etiology was tuberculosis
1933	Neumann[26]	Phlyctenules of conjunctiva	Tonsillectomy performed as part of treatment
1934	Nobécourt and Ducas[27]	Phlyctenularlike lesions of conjunctiva	Suggested etiology was hyperallergy to tuberculosis
1934	Niklasson[28]	Tuberculous ulcer of conjunctiva (biopsy)	Skin lesions appeared first
1935	Feigenbaum[29]	Episcleritis and keratitis	Suggested tuberculous etiology. Ocular lesions thought to be metastatic
1937	Blobner[30]	Bilateral iritis and right hypopyon	Patient also had right central tuberculous choroiditis. Erythema nodosum occurred in 2nd year of a 5–6 year period of recurrent iritis after which the right eye was enucleated
1939	Greene and Perry[31]	Bilateral nodules of conjunctiva over insertions of all recti muscles	Ocular and skin lesions occurred simultaneously 2 months after a tonsillectomy. Arthralgia present also
1939	Tatár[32]	Retinitis pseudonephritica and periarteritis retinas	Suggested allergy to tubercle protein as etiology
1939	Pierret, et al.[33]	Phlyctenular keratitis	Suggested allergy to tubercle protein as etiology of ocular and dermal lesions
1940	Kiesen[34]	Conjunctival nodules	Suggested etiology was allergy to the streptococcus. Patient had rheumatism and angina pectoris
1941	Esbjerg[35]	Bilateral iridocyclitis	Patient had Boeck's sarcoid and uveoparotid fever. Skin lesions appeared first
1944	Thiers, et al.[36]	Phlyctenular conjunctivitis	Ocular and dermal lesions followed treatment of tuberculosis with thiozamide
1947	Casari[37]	Bilateral conjunctival nodules	Biopsy revealed edema and necrosis of subconjunctival tissue with perivascular lymphocytic infiltration. Patient had had dry pleurisy
1947	Casari[38]	Phlyctenular conjunctivitis	Etiology thought to be homoallergic, para-allergic, or heteroallergic reaction
1947	Casari[38]	Phlyctenular conjunctivitis	Skin and ocular lesions followed penicillin and sulfadiazine treatment for erysipelas
1947	Casari[38]	Episcleritis	Ocular lesions followed erythema nodosum by 2 months
	Titomanlio[39]	Acute glaucoma	
	Marfan[40]	Keratitis and phlyctenular conjunctivitis	
1956	Maumanee[41]	Recurrent hypopyon iritis	Patient also had genital and stomal ulcers plus arthritis

TABLE 2

PREDILECTION FOR OCULAR STRUCTURES IN REPORTED CASES OF ERYTHEMA NODOSUM

Ocular Lesions	Number of Cases
Nodules of sclera and/or conjunctiva	19
Uveitis	10
Episcleritis and/or keratitis	5
Phlyctenules	7
Miscellaneous	6
Total	47

lesions also may appear during the course of erythema multiforme, trichophytosis, lues, lymphogranuloma venereum, chancroid, sarcoidosis, rheumatic fever, meningococcemia, and coccidiodal infection.[1, 42]

CASE REPORT

C. S., a 29-year-old Negress, was admitted to Cook County Hospital on March 1, 1958, with the chief complaints of pains in her legs and redness of both eyes. Two weeks prior to admission she experienced an upper respiratory infection. One week prior to admission painful lumps appeared on her shins and both eyes became red, though she experienced no loss of vision.

Examination of this well-developed and well-nourished, afebrile, normotensive female showed abnormalities limited to the eyes and lower extremities. Each eye had a visual acuity of 20/20. In the interpalpebral fissure of the left eye, extending from the semilunar fold to the limbus, was an area of conjunctival hyperemia in the center of which were tan, nodular, compartmented, painless, episcleral masses (fig. 1). The right eye had lesions similar in appearance and location but the reaction was less intense; only a small area of hyperemia surrounded a single nodule of the episclera (fig. 2). Tenderness as well as photophobia and signs of uveitis were absent. The optic discs, maculas, and retinal vessels were normal.

From the knees to the ankles of both lower extremities over the skin of the anterior tibia, dark red, elevated, tender and indurated, nonmovable lesions were observed. These varied in diameter from three to 30 mm. (fig. 3). The chest X-ray film was negative. The skin reaction from old tuberculin was three-plus but that from blastomycin and coccidioidin was negative. The diagnosis was erythema nodosum with associated episcleral nodules. Biopsy of the lesion on the left eye was done on March 4, 1958.

Treatment consisted of oral tetracycline, aspirin, antibiotic eyedrops, and cortisone eyedrops. Twelve

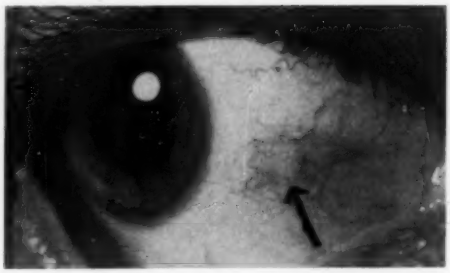


Fig. 2 (McCarthy). Appearance of right eye about 10 days after onset of ocular lesions. Intensity and size of lesion less than in left eye. Arrow points to the nodule.

Fig. 1 (McCarthy). Appearance of left eye about 10 days after onset of ocular lesions. Confluent nodules are located between the limbus and the semilunar fold. Arrow points to the nodule.

Fig. 3 (McCarthy). Appearance of scattered anterior tibial lesions about 10 days after their onset.

Fig. 4 (McCarthy). Photograph of both eyes about 33 days after the onset of the patient's illness. Shows some resolution after 23 days of treatment with topical antibiotics and corticosteroids.

days after admission the ocular and skin lesions showed signs of resolution. By March 23, 1958, the conjunctiva of the left eye was mildly hyperemic and no nodules were present (lesion biopsied) (figs. 4 and 5). At that time the right eye showed nasal bulbar conjunctival hyperemia and a tiny, tan nodule (figs. 4 and 6). The lesions of the lower extremities were smaller, pigmented, nontender and not elevated above the surface of the skin (fig. 7). By mid-May, approximately three months after the disease had begun, the hyperemia of the conjunctiva was about gone and a tiny nodule remained on the right eye (figs. 8, 9, and 10). The skin lesions on the lower extremities were barely visible (fig. 11). In June, only a trace of hyperemia of the conjunctiva of both eyes remained. At her last visit to the Cook County Hospital eye clinic in July, 1959, both eyes were normal.

Histopathologic findings

The excised tag of superficial sclera and conjunctiva was fixed in 10-percent formalin after which it was sectioned in paraffin and colored with hematoxylin and eosin, silver,

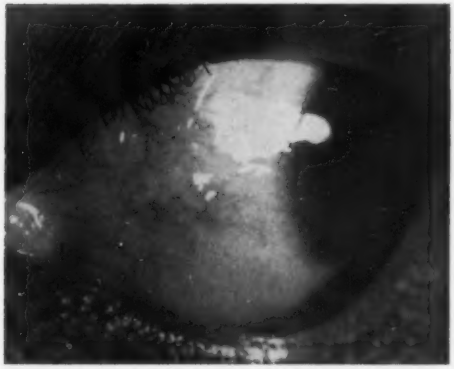


Fig. 5 (McCarthy). Close-up of left eye about 33 days after onset of ocular lesions. Site of biopsy is in center of hyperemic area.

Fig. 6 (McCarthy). Close-up of right eye about 33 days after onset of ocular lesions. Hyperemia and diminutive nodule persist. Arrow points to nodule.

connective tissue and PAS stains. The conjunctival epithelium was edematous and there was an increased amount of mucus; hyperemia, edema, perivascular lymphocytic infiltration, and interstitial dispersion of plasma cells and small macrophages characterized the reaction pattern of the adenoid and fibrous layers of the submucosa. The basement membrane was not thickened. No sign of nodules, follicles, or granulomas was present (figs. 12 and 13).

The episcleral nodule had a lighter-staining periphery and a darker staining core

Fig. 7 (McCarthy). Photograph of anterior surface of both legs. Slight pigmentation of the skin lesions remains. Appearance about 33 days after onset of patient's illness and after treatment with oral tetracycline over a 20-day period.

Fig. 8 (McCarthy). Appearance of both eyes approximately three months after onset of illness.

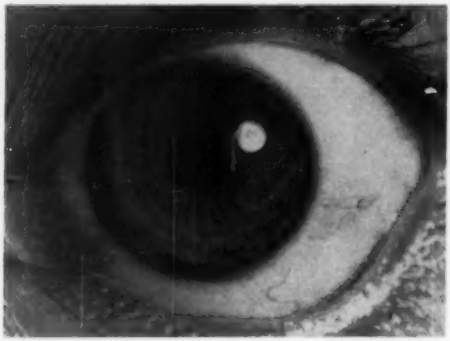


Fig. 9 (McCarthy). Close-up of left eye about three months after onset of lesions. Resolution is about complete.

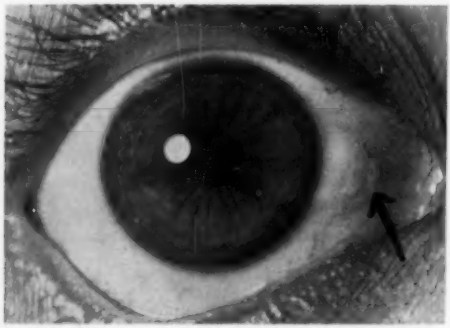


Fig. 10 (McCarthy). Close-up of right eye about three months after onset of lesions. A tiny nodule remains. Arrow points to nodule.

(fig. 14). Though suggestive no definite mesothelial lining was seen about the nodule. Its edematous periphery was infiltrated with small macrophages, lymphocytes, diminutive fibrocytes, and an occasional plasma cell; no giant cells were seen though small capillaries were present (fig. 15). The cell population of the center of the nodule was more dense. Scattered about much nuclear debris and amorphous material were small macrophages, fibrocytes, and an occasional plasma cell and lymphocyte (fig. 16). No eosinophiles were seen. The initial inflammatory reaction apparently was located in areas such as these. The tissue adjacent to the nodule showed lymphocytic perivascular

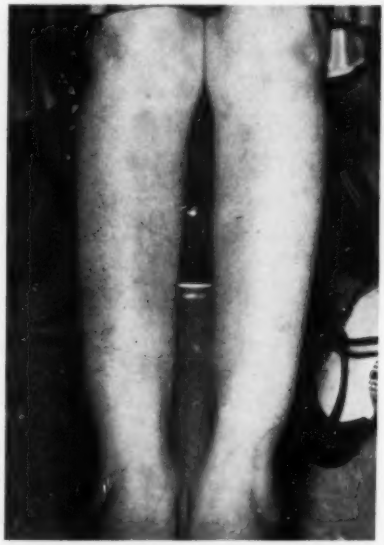


Fig. 11 (McCarthy). Appearance of legs about three months after onset of erythema nodosum. Pigmentation of lesions is about gone.

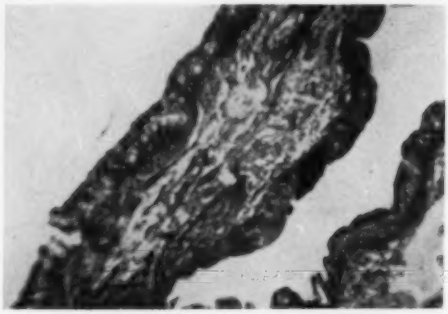


Fig. 12 (McCarthy). Low-power photomicrograph of conjunctiva overlying nodular lesion. Slightly out of focus but demonstrates that the nodules are not in the conjunctiva. (Connective tissue stain.)

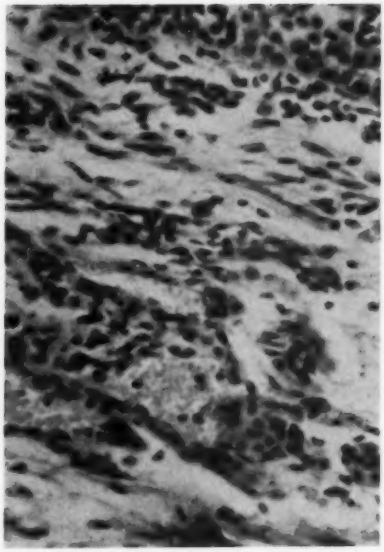


Fig. 13 (McCarthy). High-power photomicrograph of conjunctiva overlying nodular lesion. The epithelium is slightly edematous. Edema, hyperemia, and perivascular lymphocytic and other round-cell infiltrates characterize the reaction in the submucosa. (Hematoxylin-eosin.)

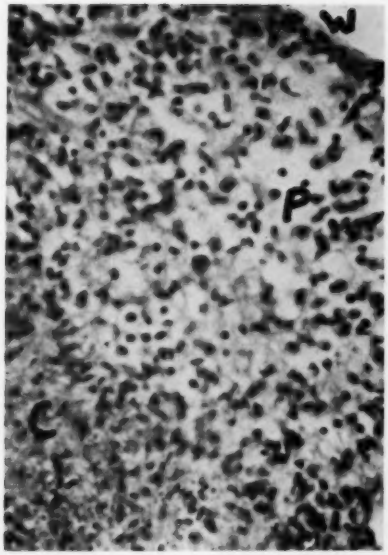


Fig. 15 (McCarthy). High-power photomicrograph of nodule. (W) Wall-like structure; (P) pale-staining periphery; (C) darker staining core. The edematous periphery is infiltrated with small fibrocytes, plasma cells, lymphocytes, and small macrophages. (Hematoxylin-eosin.)

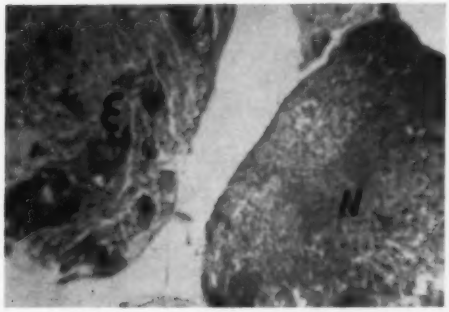


Fig. 14 (McCarthy). Low-power photomicrograph of nodule (N) and episclera (E). Out of focus. (Hematoxylin-eosin.)

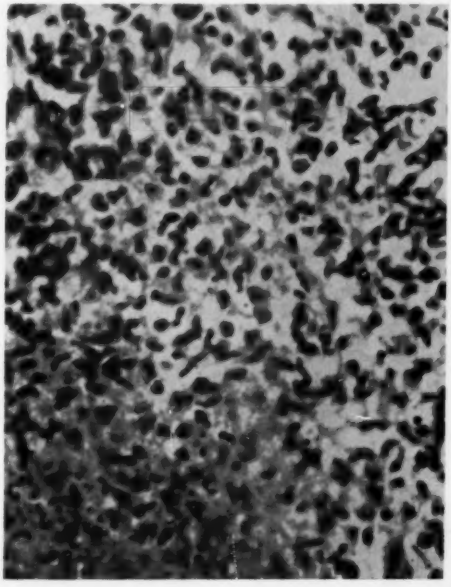


Fig. 16 (McCarthy). High-power photomicrograph of central area of nodule. Shows denser cellular infiltrate of round cells, small fibrocytes, nuclear debris and amorphous substance. (Hematoxylin-eosin.)

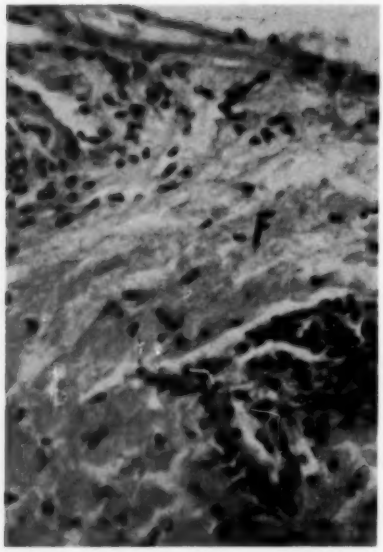


Fig. 17 (McCarthy). High-power photomicrograph of adjacent superficial scleral tissue. Perivascular round cell infiltrates are present. (F) Suggestive area of fibrinoid degeneration. (Hematoxylin-eosin.)

Fig. 19 (McCarthy). Low-power photomicrograph of nodule which shows latticelike arrangement of elastic tissue about the nodule. Elastic tissue is present within the nodule (N) but in an amorphous form.

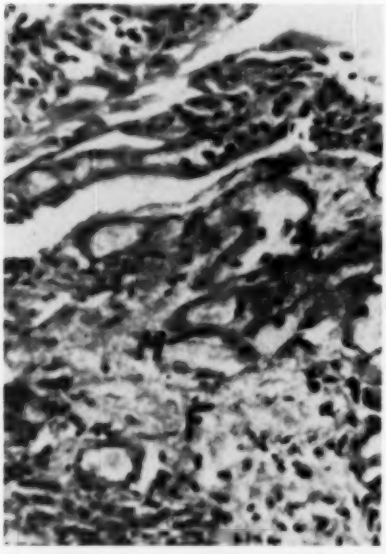


Fig. 18 (McCarthy). High-power photomicrograph of adjacent episcleral tissue. Shows thickening of arterial basement membrane (M). (F) Suggestive areas of fibrinoid degeneration. (PAS stain.)

infiltration and suggestive areas of fibrinoid degeneration (fig. 17); patchy thickening of arteriolar basement membrane was seen in some of these areas (fig. 18). A dense latticelike network of elastic tissue was dispersed about the periphery of the nodule but, centrally, the amorphous content of the lesion showed no typical organized elastic fibers (fig. 19). The PAS stain showed a darker central area in the nodule which contrasted with the lightly colored periphery (fig. 20). Connective tissue elements were dense in the periphery of the lesion but very sparse centrally (fig. 21).

Discussion

Streptococcal infections probably are the most common single cause of erythema nodosum.[1] Though presumptuous, the simultaneous occurrence of skin and eye lesions following an upper respiratory infection supports that contention in this case. That both the erythema nodosum and the epi-

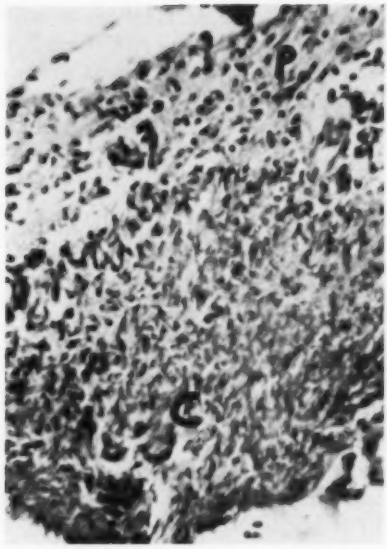


Fig. 20 (McCarthy). Low-power photomicrograph of nodule. The periphery (P) takes a less intense stain in comparison with the central area (C). (PAS stain.)

scleral nodules are caused by the same agent is difficult to refute. The fact that the patient had a positive skin test to old tuberculin must not be entirely disregarded but the negative chest X-ray film, absence of typical phlyctenules and deep scleral nodules, and the failure to find granulomas or phlyctenules in the histopathologic sections tend to discredit tubercle protein as a likely etiologic agent in this case.

Past authors have suggested rheumatism[10, 15, 21] tuberculosis,[11, 13, 15, 21, 22, 25, 27, 28, 32, 33, 37] syphilis,[15] streptococcal infections,[34, 38] and drugs (thiozamide[36]), (penicillin and sulfadiazine[36]) as the etiologic process or agents of the ocular components of erythema nodosum. Though emphasis had been placed on embolic and metastatic phenomenon from the skin as the mechanism for the ocular lesions,[7, 8] recent authors[27, 32, 33, 34, 37, 38] tend to support an allergic basis for the inflammatory reaction, the most common allergens being tubercle protein, the streptococcus, and sulfonamides.

It has been suggested that this hypersensitive reaction in the ground and cement substances of collagen tissue is characteristic of a group of diverse processes called collagen diseases, examples of which are erythema nodosum, periarteritis nodosa, dermatomyositis, scleroderma, disseminated lupus erythematosus, rheumatic fever, and rheumatoid arthritis.[43] Due to the benign, self-limited course of erythema nodosum, along with its typical location and failure in most instances to recur, it is debatable whether or not this disease should be classified with such chronic, recurring, and often fatal morbid processes.

Both skin and scleral lesions in this case had a similar appearance—erythema and nodule formation. Both appeared and disappeared simultaneously. However, past experience of others has shown that either the skin or eye lesions may occur first and that no definite pattern in their appearance is seen.[3, 5, 30] Why the most common ocular finding in this disease, namely episcleral

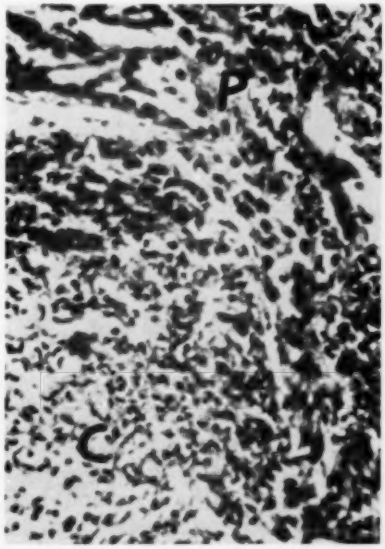


Fig. 21 (McCarthy). Low-power photomicrograph of nodule. Connective tissue elements are more dense in the periphery (P) than in the central area (C). (Connective tissue stain.)

nodules, usually is located in the palpebral fissure commonly near the insertion of the medial rectus is unknown. Uveitis associated with erythema nodosum affects predominantly the anterior segment, usually is nongranulomatous in appearance, frequently is associated with hypopyon, and has a tendency to bilaterality.

Nodular episcleritis, pingueculum, granulomatous conjunctivitis, and conjunctival phlyctenules should be considered in the differential diagnosis.

Nodular scleritis is a form of granulomatous scleritis which may be due to tuberculosis, syphilis, or sarcoidosis. There is usually some degree of uveitis present, though vision may be little affected. The onset is usually insidious and frequently only a sector of the sclera is involved. Unilateral cases are more frequent than bilateral ones, and the course of the disease is long. The episcleral nodules associated with erythema nodosum have a rapid onset, the lesions are more superficial and are smaller, there is a tendency to bilaterality, the course of the disease is shorter and more benign, and granulomas are not seen in the histopathologic sections.

The nonhyperemic pingueculum is usually located closer to the limbus and has more of a plaquelike appearance. The granulomatous conjunctivitides are accompanied by a diffuse inflammatory reaction in which ulceration and necrosis may be conspicuous. Preauricular adenopathy often is present. The large single granulomas of rhinosporidiosis may require microscopic examination and a culture.

The slightly elevated, gray and, at times, ulcerated lesions of phlyctenules of the conjunctiva have a propensity for the limbus and frequently involve the adjacent cornea. Photophobia, absent in episcleral nodules associated with erythema nodosum, is almost necessary for the diagnosis.

Histopathologic evidence in this case supports the contention that the most likely site of the initial inflammatory reaction was in the connective tissue of episclera or superficial sclera. Following the initial insult, the connective tissue framework was destroyed and a small nidus of amorphous material and nuclear debris formed the central mass of a nodule. The cellular infiltrate was nonspecific, consisting for the most part of small macrophages (fig. 16). Connective tissue elements were sparse (fig. 21) and the elastic tissue framework was destroyed (fig. 19). Also the PAS stain was more intense (fig. 20). Edematous connective tissue, scattered areas of fibrinoid degeneration, and nonspecific small round-cell infiltrates completed the structure of the periphery of a nodule (figs. 15, 17, and 18).

The similarity of these nodules to the Aschoff body of rheumatic endocarditis and to the subcutaneous nodules of rheumatic fever is striking. An Aschoff body is a nodule commonly located in the loose connective tissue near a coronary arteriole. A central mass of swollen, hyalinized necrotic collagen is surrounded by a coronet of mononuclear cells. The nodule goes through a definite cycle, the characteristic Aschoff cell, a large cell with basophilic cytoplasm and a large nucleolus (owl-eyed cell), appearing in the middle stages. Subcutaneous nodules of rheumatic fever are painless and produce no symptoms. A central area of necrosis is present, due to fibrinoid swelling. A middle zone is comprised of large mononuclear cells in palisade or radial arrangement. There is no connective tissue capsule present which makes the periphery of the lesion indistinct.[44]

Dilatation of vessels, perivascular infiltrates of polymorphonuclear cells, and edema of the dermis constitute the microscopic findings in skin lesions of erythema nodosum.

Casari[37] reported the pathologic findings in a case of conjunctival nodules associated with erythema nodosum. Edema and necrosis of the subconjunctival tissue along with perivascular lymphocytic infiltration were observed. Palisading of monocytes along scleral fibers and fibrinoid degeneration were

observed by Maumenee[41] in a case of a nodule of the sclera in scleritis.

Treatment of the disorder is elimination of the offending cause, if one is found or clinically suspected. Most commonly this would consist of treating a streptococcal infection. Systemic corticosteroids are not recommended.[1] Episcleral nodules are treated with topical corticosteroids. When uveitis occurs, treatment with atropine and corticosteroids, topical and/or systemic is indicated.

The prognosis in these cases, except when the uveal tract has become inflamed, is uniformly good. One can expect complete disappearance of the nodules and hyperemia without residue.

Summary

A case report and histopathologic observations of superficial nodules associated with erythema nodosum are presented. In each eye in the interpalpebral fissure small episcleral nodules in a patch of conjunctival hyperemia were observed between the limbus and the semilunar fold. It is suggested that the ocular and skin lesions were excited by the same agent, most likely the streptococcus and, further, that the inflammatory lesion per se is an allergic one, occurring in the connective tissue of the episclera and/or the superficial sclera. The overlying conjunctiva was secondarily involved. The biopsied nodule showed a central core of necrotic, amorphous tissue surrounded by edematous connective tissue with nonspecific round-cell infiltrates and occasional patches of fibrinoid degeneration. The lesion appeared similar to Aschoff and subcutaneous nodules seen in rheumatic fever. Though the lesions under consideration occur in collagen tissue the reaction panorama should not be considered one of the collagen diseases.

6429 West North Avenue.

References

1. Pillsbury, D. M., Shelley, W. B., and Kligman, A.: Dermatology. Philadelphia, Saunders, 1956, pp. 948-949.
2. Beaudonnett, B.: Contribution a l'étude des manifestations oculaires dans l'érythème polymorphe. Thèse de Paris, Henri Jouve, 1894. (Cited by Greene and Perry.[31])
3. Brault, J.: Erythème polymorphe récidivant, association des formes papuleuse et noueuse, papules conjonctivales en gros placards. Soc. derm. & syph. (Apr.), 1896. (Cited by Chaillous.[6])
4. Schneider, G.: Des manifestations oculaires de l'érythème noueux febrile (conjunctivite et épisclérite aiguë). Rec. ophtal., **7**:395, 1899. (Summarized by Ostwalt, F.: Zschr. f. Augenh., **4**:313, 1900.)
5. Allan, A. W.: Erythema nodosum complicated with iritis. Brit. M. J., **2**:1267, 1901.
6. Chaillous, J.: Étude clinique des lésions conjonctivales au cours de l'érythème polymorphe. Ann. ocul., **127**:173-183, 1902.
7. Schein, M.: Relation entre l'épisclérite d'un côté et l'érythème exsudatif multiforme et l'érythème noueux de l'autre côté. Pester médicin. Chirurg. Presse, pp. 981, 1005, 1904. (Summarized in Ann. ocul., **133**:75-76, 1905.)
8. Reis, W.: Augenerkrankung und Erythema nodosum. Klin. Monatsbl. f. Augenh., **44**:203-223, 1906.
9. Burnand: Un cas d'érythème noueux et polymorph avec complications oculaires. Revue méd. dela Suisse romande, (Oct.), 1907. (Summarized in Jahres bericht über die Ophth., **38**:399, 1907.)
10. Lurie, O. R.: Doppelseitige plastische Iritis bei Erythema nodosum. Ztschr. f. Augenh., **24**:458-462, 1910.
11. Terson: Lésions oculaires dans l'érythème polymorphe; noueux et tuberculose; érythème noueux et glaucome. Arch. ophtal., **32**:274, 1912. (Summarized in Klin. Monatsbl. f. Augenh., **50**:381-382, 1912.)
12. Weil, E., Chevallier, P., and Toulant, P.: Sur la fréquence des lésions oculaires au cours de l'érythème noueux. Bull. et mém. soc. méd. hôp. Paris, **30**:524-526, 1914. (Summarized by Teich: Zentralbl. f. ophth. & Grenzgbt., **1**:329, 1914.)
13. Haab, O.: Neue Beobachtungen an Hornhaut und Netzhaut. Med. Klinik, **27**:(Jul.) 1916. (Summarized in Klin. Monatsbl. f. Augenh., **57**:217-218, 1916.)
14. Gilbert, V. W.: Ueber Ringknoten des Ziliarkörper bei Erythema nodosum. Arch. f. Augenh., **85**: 50-54, 1919.
15. Satanowsky, P.: Augenkomplikationen des Erythema nodosum. Semana med., **30**:33-37, 1923. (Summarized by Hachez, E.: Zentralbl. f. Haut-u. Geschlechtskrankh., **8**:396, 1923.)
16. Weltistscheff, F.: Erythema nodosum conjunctiva bulbi. Russk. Ophth. J., **6**:619-621, 1925. (Cited by Greene and Perry.[31])

17. Kaznelson, A.: Rezidivierende Hypopyon-Iritis (Iritis septica) and Erythema nodosum. Russk. Ophth. J., **4**:484-491, 1925. (Summarized by Paldrock: Zentralbl. f. Haut-u. Geschlechtskrankh., **22**:774, 1927.)

18. Cavara: Cited by Casari.[39]

19. Fuchs, A.: Ueber chronische multiple Knotenbildung am Körper mit häufig rezidivierender eitriger Iritis und Scleritis. Otsch. med. Wchnschr., **52**:1503-1505, 1926.

20. Tow, A.: Erythema nodosum and phlyctenular conjunctivitis in a case of hilus gland tuberculosis. Arch. Pediat., **45**:687-691, 1928.

21. Rotth, A. V.: The involvement of the cornea in erythema nodosum. Ztschr. f. Augenh., **66**:323-327, 1928. (Summarized by Haessler, F. H.: Am. J. Ophth., **12**:342, 1929.)

22. Josefsen, A., and Malmgren, G.: On the initial exanthema and enanthema of tuberculosis. Acta med. scand. (suppl.) **26**:196-221, 1928.

23. Rameev, R.: Ophthalmologische Beobachtungen. Russk. Ophth. J., **11**:815-822, 1930. (Cited by Greene and Perry.[31])

24. Shieck, F.: Die Erkrankungen der conjunctiva, cornea, und sclera. Kurzes Handb. Ophth., **4**:112-117, 1931. (Cited by Greene and Perry.[31])

25. Krachmalnikov, L.: Erythema nodosum conjunctivum bulbi. Arch. f. Ophth., **8**:184-186, 1932. (Cited by Greene and Perry.[31])

26. Neumann, W.: Phlyctäne, Erythema nodosum und Pancetscher Rheumatismus. Med. Klin., **29**:1407-1408, 1933.

27. Nobecourt, P., and Ducas, P.: Erythème noueux et conjonctivite phlycténulaire. Presse méd., **42**: 1241-1242, 1934.

28. Niklasson, H.: Primary tuberculosis of the conjunctiva with erythema nodosum. Acta. Ophth., **12**: 244-248 (Pt. 3) 1934. (Summarized by Daily, R. K.: Am. J. Ophth., **18**:478, 1935.)

29. Feigenbaum, A.: On typical and atypical episcleritis forms and their relations to rheumatic episcleritis and to erythema nodosum. Folia Ophth. Orienta, **2**:27, 1935. (Summarized by Grunfeld, R.: Am. J. Ophth., **19**:1132, 1936.)

30. Blobner, F.: Zur rezidivierenden Hypopyoniritis. Ztschr. f. Augenh., **91**:130-139, 1937.

31. Greene, L. S., and Perry, M. W.: Erythema nodosum with nodules in the conjunctivae. Am. J. Ophth., **22**:389-391, 1939.

32. Tatár, J.: Retinitis pseudonephritica and Periarteritis retinae anschliessend an Erythema nodosum. Klin. Monatsbl. f. Augenh., **103**:84-91, 1939.

33. Pierret, R., Breton, A., and Lefebvre, G.: L'érythème noueux et la kératite reflet des variations de l'allergie tuberculeuse chez l'enfant. Paris méd., **1**:255-257, 1939. (Summarized by Keller, W.: Zentralbl. f. Haut-u. Geschlechtskrankh., **63**:274, 1940.)

34. Kiesen, E. G.: Erythema nodosum with involvement of the conjunctiva. Viestnik. Ophtal., **16**:506 (Pt. 6), 1940. (Summarized by Daily, R. K.: Am. J. Ophth., **24**:465, 1941.)

35. Esbjerg, H. O.: A case of uveoparotid fever attended by erythema nodosum and pulmonary changes. Acta Ophth., **19**:286-292 (Pt. 3-4), 1941.

36. Thiers, H., Raccuchot, and Vignon: Erythème noueux avec conjonctivite phlycténulaire déclenché par le thiozamide chez un ancien tuberculeux chirurgical. Ann. derm. & syph., **4**:110 (8th series), 1944.

37. Casari, G. F.: Reperto istologico di efflorescenza cogiuntivale di eritema nodosa. Rassegna ital. òttal., **16**:467-472, 1947.

38. ———: Le manifestazioni oculari nel corso dell'eritema nodoso. Rassegna ital. òttal., **16**:228-250, 1947.

39. Titomanlio: Cited by Casari.[39]

40. Marfan: Cited by Casari.[39]

41. Maumanee, A. E.: Ocular manifestations of collagen diseases. Arch. Ophth., **56**:557-562, 1956.

42. Sutton, R. L., and Sutton, R. L., Jr.: An Introduction to Dermatology. St. Louis, Mosby, 1941, pp. 94-96.

43. Adler, F. H.: Gifford's Textbook of Ophthalmology. Philadelphia, Saunders, 1953, ed. 5, p. 243.

44. Anderson, W. A. D.: Pathology. St. Louis, Mosby, 1948, ed. 1, pp. 498-499.

SCLEROMALACIA PERFORANS AND MASSIVE GRANULOMA OF THE SCLERA*

A REPORT OF AN UNUSUAL COMBINATION OF OCULAR PATHOLOGY IN RHEUMATOID ARTHRITIS

J. REIMER WOLTER, M.D.
Ann Arbor, Michigan
AND
MAXWELL D. BENTLEY, M.D.
Cadillac, Michigan

Three main types of scleral involvement in rheumatoid arthritis can be distinguished: the massive granuloma of the sclera, necroscleritis nodosa, and scleromalacia perforans. Basically all these lesions are considered rheumatoid nodules of the sclera (Ashton and Hobbs[1]). However, distinct differences in their location and the associated degree of scar formation separate the three conditions in their clinical and pathologic aspects.

Massive granuloma of the sclera (Derby and Verhoeff[2]) which is also known as brawny scleritis, scleritis posterior, annular scleritis (Berens[3]) or fusiform sclero-uveitis (Contardo[4]) involves large areas of sclera and goes along with massive scar formation.

Necroscleritis nodosa (Edstroem and Oesterlind[5]) is limited to small areas of the anterior sclera and results in the formation of prominent nodules.

Schleromalacia perforans (Van Der Hoeve[6]), finally, is also limited to small areas of the anterior sclera but shows little scar formation and results in round scleral defects.

All three scleral diseases are chronic, slowly progressive, painful, and resistant to treatment. Their course often shows remissions and exacerbations and in many cases finally leads to a blind painful eye.

All three of the scleral involvements of rheumatoid arthritis just mentioned are not rare. However, it seems that in all known cases only one type of these rheumatoid scleral involvements is found in one eye. The present demonstration includes two cases in both of which a combination of scleromalacia perforans and massive posterior scleritis occurred in the same eye.

* From the Department of Ophthalmic Surgery and the Laboratory of Neuropathology of the University of Michigan Medical Center. This study was supported by Grant No. B-2873 of the U. S. Department of Health, Education and Welfare.

CASE REPORTS

CASE 1

This 73-year-old white man was first seen on May 14, 1959. He gave a history of having had "arthritis" for about 25 years. This involved his knees, hips, hands and shoulders. It would be sometimes in one joint and sometimes in several joints. He had been hospitalized for this and the diagnosis of rheumatoid arthritis had been made several years ago. At the time of this examination the patient complained of pain in his joints and his movements were extremely slow and labored because of this.

His left eye had become red about three months before. Within the last three weeks before this examination the left eye had become blind and extremely painful.

The eye examination showed an externally normal right eye. The left eye was deeply injected, tender, and hard and also exhibited extreme limitation of movement in all directions of gaze. The visual acuity was O.D., 20/200; O.S., light perception only. Intraocular pressure was: O.D., 20 mm. Hg; O.S., 46 mm. Hg (Schiøtz) with a 10-gm. weight. The media of the right eye were clear. The right fundus showed a normal disc. The retina exhibited central and peripheral degeneration of the senile type and advanced sclerotic vascular changes. The left cornea was somewhat cloudy but the media were otherwise clear. The pupil could not be well dilated. The left fundus showed a massive retinal detachment inferiorally and nasally. The periphery could not be seen.

A malignant melanoma of the choroid was considered a possible cause of the solid retinal detachment in the blind and painful left eye. Immediate enucleation was suggested. This was performed on May 15, 1959. During surgery great difficulties were encountered to rotate the eye and a dense cartilagelike mass was found adherent to the globe

as well as to the orbital tissues. No implant was used following the enucleation because it was felt that the indurated ocular socket would not tolerate it.

The day following this surgery the patient began having severe pain in his arms and legs; later the same day he became incontinent and finally comatose. He was treated with Sola-Cortef intravenously and improved slowly until he could be dismissed five days following the enucleation. The patient was seen again May 25, 1959, and the socket was found to be healing nicely. However, the patient was virtually immobile because of pains in all his joints. Blood was drawn at this time and sent to the Arthritis Clinic of this University Medical Center to do the Ziff procedure for rheumatoid factor. This was found to be positive with 1/56.

The left eye was fixed in formalin immediately after enucleation. The globe was of about normal size. A bluish defect in the sclera filled with whitish tissue and measuring about three mm. in diameter was seen next to the limbus at the 8-o'clock position. After opening the globe, a large area of the posterior and temporal sclera was found to be extremely thickened and of a dense scarlike consistency. Figure 1 shows a low-power view of a section through the middle of the thickened sclera in the upper half of the globe.

This thickening involved the choroid, sclera and episcleral tissues. It extended to the optic nerve but did not involve it. There is also an area of exudative retinal detachment visible in this section. Figure 2 shows a section of the lower half of the globe which exhibited also some scleral thickening posteriorly. Two areas of exudative retinal detachment are also seen.

Fig. 1 (Wolter and Bentley). *Case 1.* Low-power view of section of upper half of globe. (a) Area of massive granuloma of sclera, (b) optic nerve, (c) exudative retinal detachment. Lens was removed before imbedding. (Paraffin section, hematoxylin-eosin.)

Fig. 2 (Wolter and Bentley). *Case 1.* Low-power view of section of lower half of globe. (a) Marginal area of massive scleral granuloma. There are two areas of exudative retinal detachment. The arrow points to the area which is seen in Figures 3 and 4 at higher power. Lens was removed before sectioning. (Paraffin section, hematoxylin-eosin.)

This power does not allow for the demonstration of details of the anterior sclera. Figures 3 and 4, however, show higher-power views of the limbus area seen on the right side of Figure 2 (arrow). These pictures show extensive thinning, interruption, and necrosis and sequestration of the sclera next to the limbus. The bundles of necrotic scleral collagen were surrounded by dense accumulations of mononuclear cells, mainly lymphocytes and plasma cells (arrow in figs. 3 and 4). There were rows of histiocytes next to degenerating bundles of scleral collagen. However, no giant cells were found in this area.

Figures 5, 6, and 7 show high-power views of the defects in the necrotic sclera which were found in the localized area next to the limbus that had macroscopically appeared as a bluish spot. In the sections all the scleral defects were found to be filled with loose scar tissue and massive mononuclear infiltration which contained a few polymorphonuclear leukocytes in some areas. This localized process next to the limbus was considered to represent a typical late stage of a scleromalacia perforans.

The cornea of this globe was about normal. The

Fig. 3 (Wolter and Bentley). *Case 1.* Area of scleromalacia perforans at the limbus at the 8-o'clock position. The arrow points to the thin layer of remaining sclera most of which is necrotic. This is surrounded by granulation tissue. (Paraffin section, hematoxylin-eosin.)

Fig. 4 (Wolter and Bentley). *Case 1.* Marginal section through the area of scleromalacia perforans at the limbus. The arrow points to the areas of scleral necrosis. (Paraffin section, hematoxylin-eosin.)

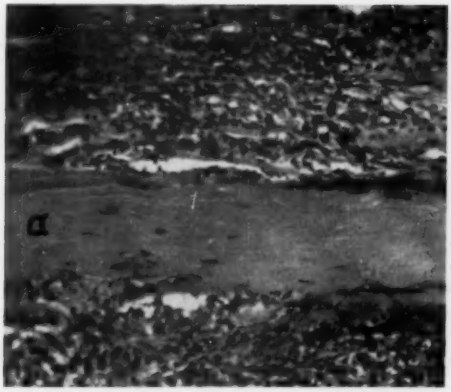


Fig. 5 (Wolter and Bentley). *Case 1.* High-power view of a necrotic piece of sclera in the area of scleromalacia perforans. Lymphocytes, histiocytes, and polymorphonuclear leukocytes are seen to surround this. (a) Necrotic collagen bundles of sclera. (Paraffin section, hematoxylin-eosin.)

anterior chamber and chamber angle appeared also normal. However, the filtration network was filled with mononuclear inflammatory cells and also showed advanced destruction in the area of the scleromalacia perforans already described. The iris and ciliary body exhibited diffuse infiltration with lymphocytes and plasma cells. The retina was atrophic (figs. 8, 9, and 10). It showed a total loss of its inner layers as well as advanced destruction of the layer of the rods and cones. Dense eosinophilic exudate which contained macrophages was seen in many areas behind the detached retina (figs. 9 and 10). The pigment epithelium exhibited a very irregular pigment distribution and cellular proliferation as well as drusen formation (fig. 9).

High-power examination of the thickened posterior ocular wall (compare figs. 1 and 2) revealed this to be composed of a massive chronic productive inflammatory process which involved the choroid, sclera, and episclera (fig. 8). In the sclera and episclera this inflammatory process had some of the characteristics of a granulomatous inflammation. Accumulations of histiocytes and an occasional giant cell were seen. There were areas of necrosis and sequestration of scleral collagen which was surrounded by scar tissue and granulomatous tissue. The true sclera was thinned. The choroid showed only a dense infiltration with lymphocytes in the area of scleritis (fig. 11) but

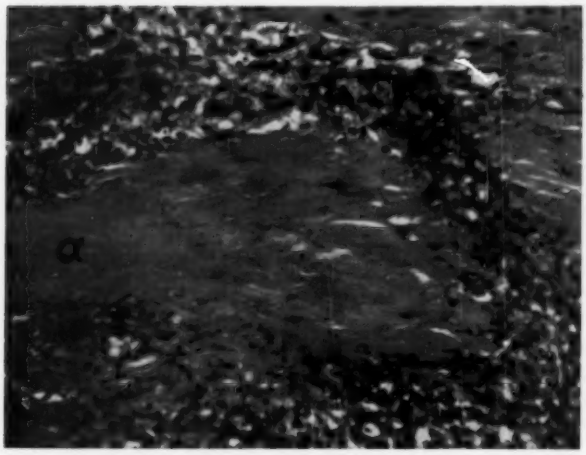


Fig. 6 (Wolter and Bentley). *Case 1.* High-power view of an area of scleral sequestration at the margin of the defect of scleromalacia perforans. The necrotic scleral tissues are seen surrounded by lymphocytes, histiocytes and some polymorphonuclear leukocytes. (a) Interrupted bundle of scleral collagen. (Paraffin section, hematoxylin-eosin.)

did not exhibit giant cells or histiocytes. Stains for the demonstration of fibrinoid materials in the scleral collagen of this globe were negative.

This latter massive involvement of large portions of the posterior ocular wall is rather typical of a late stage of the so-called massive granuloma of the sclera. There was no direct connection between the anterior area of scleromalacia perforans and the posterior massive scleritis in this eye.

CASE 2

This 65-year-old white man was first seen by Dr. C. H. Ade of Lafayette, Indiana, on October 9, 1959. He gave a general history of having had rheumatoid arthritis for the last 40 years. He had been totally incapacitated for the last three or four years. The patient stated that he had pain in his right eye and that he had become completely blind in this eye within the last year. There had been no trauma. Recently the pain had become virtually intolerable and the patient became anxious to have the eye removed.

The examination showed the eye to be completely blind. The intraocular pressure was found to be 80 mm. Hg (Schiøtz). Miotics were tried and the pressure went down to 65 mm. Hg. Since the pain persisted and the eye was totally blind, an enucleation was performed on October 10, 1959. The globe was sent to this Eye Pathology Laboratory.

Figure 12 shows the macroscopic appearance of this eye after it was opened. It was normal in size. A bluish defect with extreme thinning of the sclera was seen nasally at the limbus (arrow). The lens was in its normal position. A tremendous thickening of the whole posterior sclera was found which surrounded the optic nerve. There was extensive exudative retinal detachment.

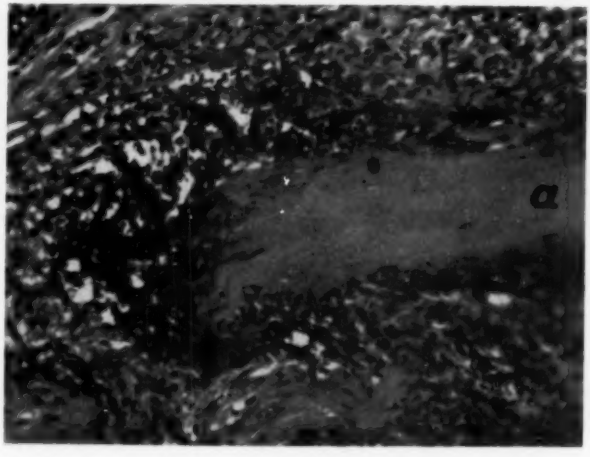


Fig. 7 (Wolter and Bentley). *Case 1.* Sequestration of necrotic sclera in the area of scleromalacia perforans. (a) Interrupted bundle of necrotic sclera. (Paraffin section, hematoxylin-eosin.)

Fig. 8 (Wolter and Bentley). *Case 1.* Low-power view of posterior ocular wall with massive scleral granuloma. (a) Atrophic retina, (b) infiltrated and thickened choroid, (c) sclera with defects and areas of granuloma, (d) infiltrated and organized episclera. (Paraffin section, hematoxylin-eosin.)

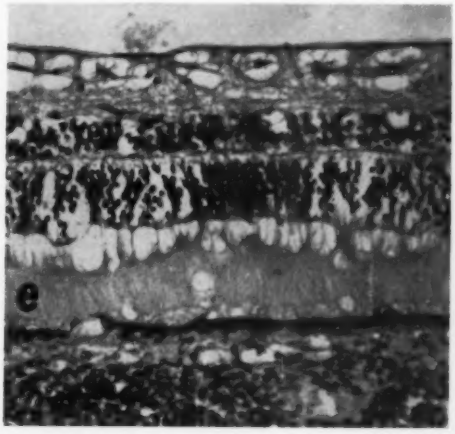


Fig. 9 (Wolter and Bentley). *Case 1.* High-power view of posterior retina. The inner retinal layers are missing. Rods and cones are destroyed. (e) Retroretinal exudate. The choroid shows dense lymphocytic infiltration. (Paraffin section, hematoxylin-eosin.)

Fig. 10 (Wolter and Bentley). *Case 1.* Low-power view of marginal area of massive scleral granuloma. The retina (a) is detached. There is retroretinal exudate (b). The choroid is thickened and infiltrated with lymphocytes (c). The sclera (d) is about normal. The episclera (e) shows mononuclear infiltration. (Paraffin section, hematoxylin-eosin.)

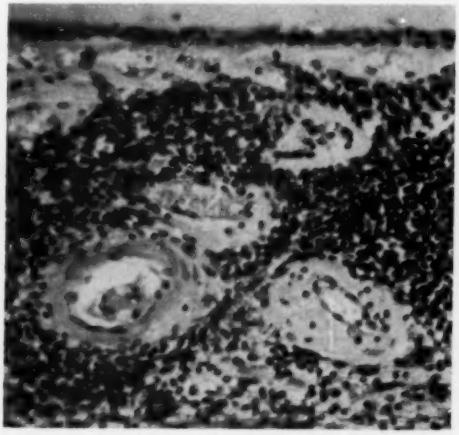


Fig. 11 (Wolter and Bentley). *Case 1.* High-power view of posterior choroid in area of massive granuloma with dense lymphocytic infiltrate. (Paraffin section, hematoxylin-eosin.)

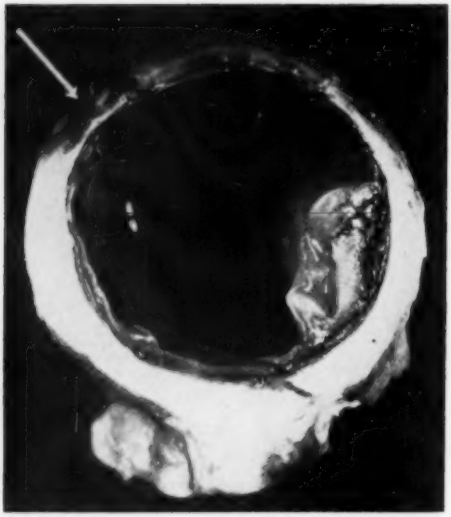


Fig. 12 (Wolter and Bentley). *Case 2.* Macroscopic view of the opened globe after removal of the lens. Arrow points to area of thinned sclera (scleromalacia perforans). The extensive thickening of the posterior sclera and the exudative retinal detachment are visible. (Paraffin section, hematoxylin-eosin.)

Figure 13 shows a section of the same eye at low power. The extensive thickening of the posterior ocular wall is seen (arrow). This involved the choroid, sclera and episclera. A large area of peripheral exudative retinal detachment is also visible.

Figure 14 shows a section of the globe at the level of the center of the macroscopically seen bluish scleral defect at the nasal limbus. This defect was almost complete (arrow) and it has become artificially perforated in this section in the histologic process. The extensive thickening which involved the whole posterior ocular wall and some exudative retinal detachment are also seen.

The cornea was about normal. The anterior chamber was shallow and the filtration angle was closed by anterior peripheral synechias. Dense infiltration with mononuclear inflammatory cells was seen in the perilimbal episclera and in the trabecular meshwork. There were also some polymorphonuclear leukocytes and plasma cells.

Nasally there was a defect in the perilimbal sclera. All of the sclera was missing in the center of this (fig. 15) where only a thin membrane of loose scar tissue was seen to cover the uvea (arrow). Scleral necrosis, thinning, and accumulation of dense granulomatous infiltration were seen in the marginal areas of this defect. Histiocytes and occasional giant cells were seen around the necrotic collagen of the sclera in this region.

The iris (fig. 16) and ciliary body showed diffuse and localized infiltration with lymphocytes and plasma cells. The same type of inflammatory reaction was seen in the peripheral choroid. The retina was detached and showed very advanced degen-

Fig. 13 (Wolter and Bentley). *Case 2.* Section through the optic nerve at low power. Arrow points to the extensive thickening of the posterior sclera (massive granuloma). There is a large area of exudative retinal detachment. (Paraffin section, hematoxylin-eosin.)

Fig. 14 (Wolter and Bentley). *Case 2.* Section through the area of scleromalacia perforans next to the limbus (arrow) which has perforated in the histologic process. (a) Massive granuloma of posterior sclera, (b) exudative retinal detachment. (Paraffin section, hematoxylin-eosin.)

eration. There were areas of extensive eosinophilic retroretinal exudate which contained macrophages. The pigment epithelium exhibited cellular proliferation and drusen formation.

The whole posterior ocular wall was involved in an extensive chronic productive inflammatory process which had its center in the sclera. It involved, however, the choroid and the episclera (fig. 17). Most of the scleral collagen bundles were missing or necrotic (fig. 18). Loose scar tissue and massive infiltration mainly with lymphocytes had replaced the scleral lamellae. However, there were also rows or nodules of histiocytes (figs. 19 and 20) and giant cells seen in this massive inflammation. The choroid was greatly thickened and exhibited dense lymphocytic infiltration. It was interesting to observe that many of the blood vessels of the organized episcleral area showed different stages of an obliterative endarteritis with fibrosis and endothelial proliferation (fig. 21). Stains for fibrinoid material were done but showed no positive reaction.

Discussion

These two cases are very similar. They represent the final stage of a combination of scleromalacia perforans and massive granuloma of the posterior sclera. Both patients suffered from advanced rheumatoid arthritis. Both had no or only insufficient eye treatment. One eye was removed because an intraocular tumor was suspected. Both eyes had secondary glaucoma and were blind and very painful.

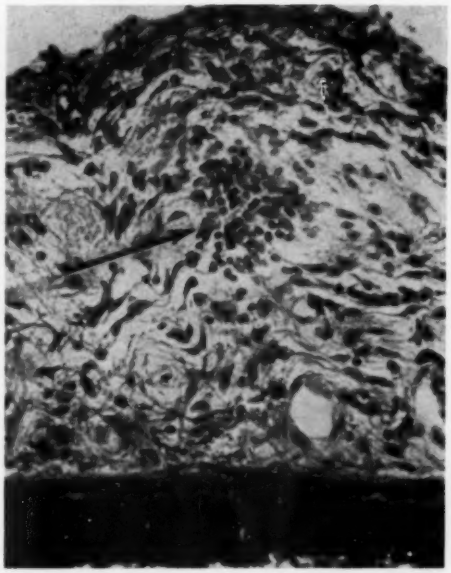


Fig. 16 (Wolter and Bentley). *Case 2.* High-power view of the iris with an accumulation of lymphocytes (arrow). (Paraffin section, hematoxylineosin.)

The importance of these two cases in that the combined occurrence of scleromalacia perforans and massive scleral granuloma indicates that these two diseases are closely re-

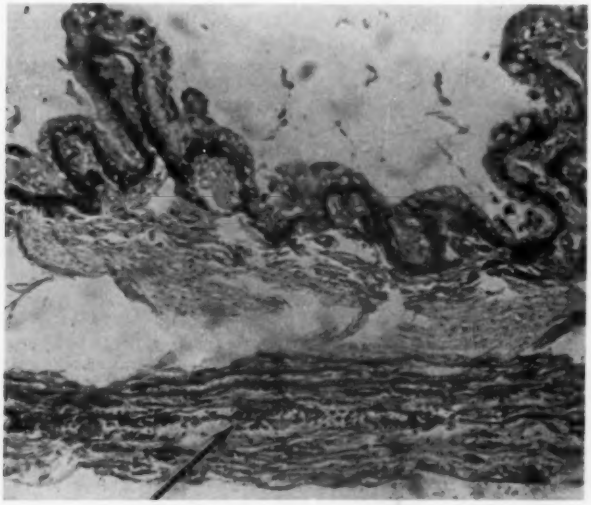


Fig. 15 (Wolter and Bentley). *Case 2.* The area of scleromalacia perforans next to the limbus. Ciliary body is seen in the upper part of the picture. Episclera (arrow) is seen below. All of the sclera is missing. (Paraffin section, hematoxylin-eosin.)

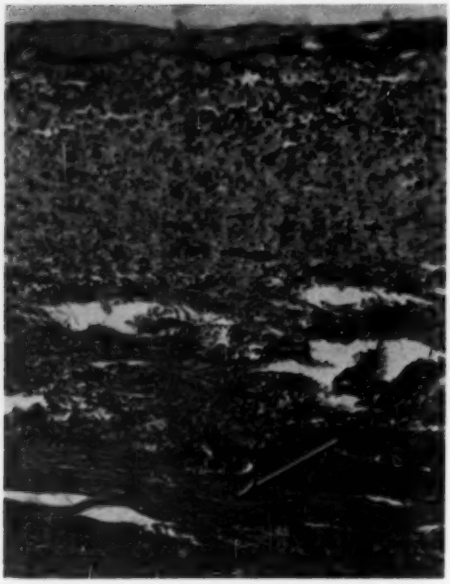


Fig. 17 (Wolter and Bentley). *Case 2.* Low-power view of posterior ocular wall in area of massive granuloma. The arrow points to remaining partially necrotic sclera which is surrounded by granulomatous tissue. The choroid is swollen and shows dense lymphocytic infiltration. (Paraffin section, hematoxylin-eosin.)

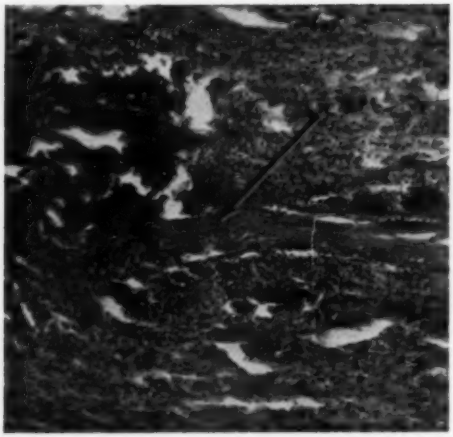


Fig. 18 (Wolter and Bentley). *Case 2.* Another area with necrosis and interruption of scleral collagen bundles (arrow) with surrounding granulomatous tissue in the area of massive granuloma. (Paraffin section, hematoxylin-eosin.)

lated. It is furthermore important to emphasize that both types of scleritis occurred in patients with advanced rheumatoid arthritis and that scleromalacia perforans is accepted as a rheumatoid involvement of the sclera.[1] Verhoeff and King[7] suggested much earlier that there is a close resemblance in the histopathology of scleromalacia perforans and massive scleral granuloma. Before their excellent paper tuberculosis and syphilis had been considered as possible causes of massive granuloma. However, none of these diseases were ever proven to be the cause in

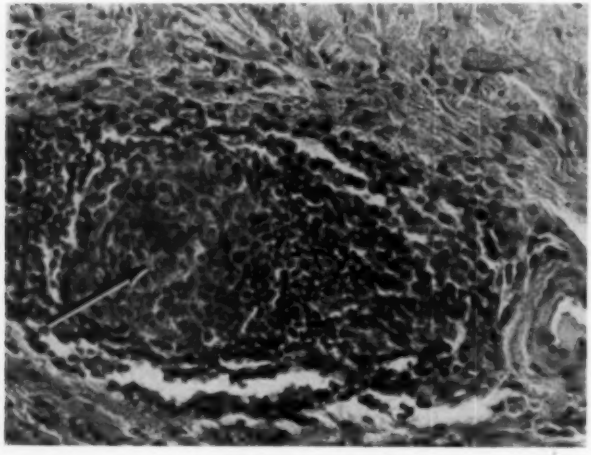


Fig. 19 (Wolter and Bentley). *Case 2.* An area of nodular arrangement of histiocytes in the massive scleral granuloma (arrow) with surrounding lymphocytes. (Paraffin section, hematoxylin-eosin.)

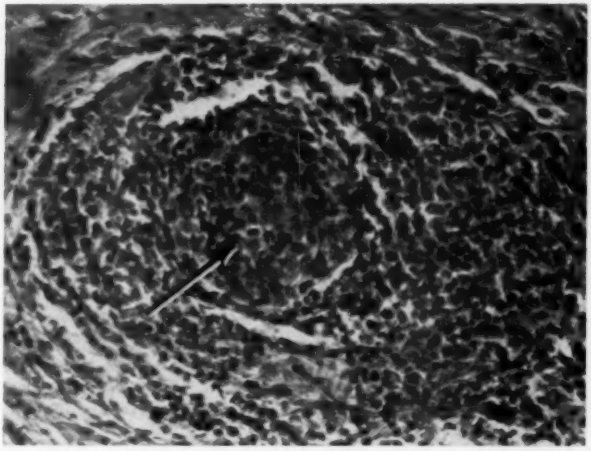


Fig. 20 (Wolter and Bentley). *Case 2.* An accumulation of histiocytes (arrow) in the area of massive granuloma of the posterior sclera. Lymphocytes and scar tissue are seen around it. (Paraffin section, hematoxylin-eosin.)

any case. In an earlier paper Derby and Verhoeff[3] therefore classified massive granuloma as a disease of unknown etiology.

The present two eyes of patients with advanced rheumatoid arthritis and a combination of scleromalacia perforans and massive scleral granuloma convinced us that massive granuloma of the sclera may occur as just another form of rheumatoid involvement of the sclera.

It must be emphasized that the histologic findings in both cases are those of a burned-out old process. No fibrinoid degeneration and no definite palisading of the typical early rheumatoid nodule were found. However, we feel that the present histologic findings still allow for a classification of all scleral involvement in these eyes as part of rheumatoid arthritis (compare Ashton and Hobbs[1]).

It seems to be quite typical that one of the eyes here demonstrated was enucleated with the diagnosis of an intraocular tumor. We have had another case of massive scleral granuloma only (Wolter and Landis[8]) that not only clinically simulated a choroidal melanoma but also had a highly positive P^{32} uptake after 24 hours. Derby and Verhoeff's[3] case was also clinically diagnosed as an intraocular new-growth.

It is our impression that the prognosis of massive scleral granuloma is very poor.[9] However, the two present cases were, of course, neglected by the patients and cannot

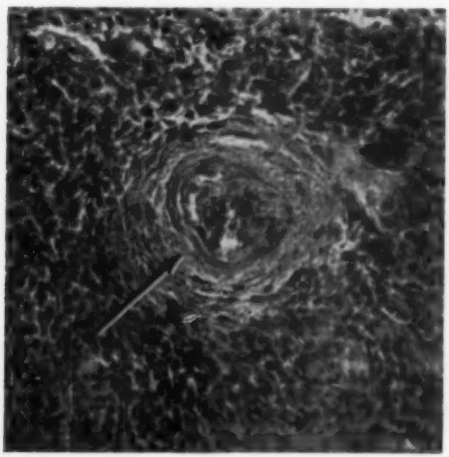


Fig. 21 (Wolter and Bentley). *Case 2.* Small blood vessel in the episclera within the massive granuloma (arrow). This exhibits fibrosis and several layers of endothelium. It is surrounded by dense granulomatous infiltration. (Paraffin section, hematoxylin-eosin.)

be used for a discussion of the proper treatment.

Summary

Two cases of a combined occurrence of scleromalacia perforans and massive granuloma of the posterior sclera in rheumatoid arthritis are reported. These cases are important since they show the close relationship of massive scleral granuloma to scleromalacia perforans. Both are considered ocular manifestations of rheumatoid arthritis.

University of Michigan
Medical Center.

References

1. Ashton, N., and Hobbs, H. E.: Effect of cortisone on rheumatoid nodules of the sclera (scleromalacia perforans). Brit. J. Ophth., **36**:373, 1952.
2. Derby, G. S., and Verhoeff, F. H.: Massive granuloma of the sclera (brawny scleritis), with the report of an unusual case. Arch. Ophth., **45**:20, 1916.
3. Berens, C.: The Eye and Its Diseases. Philadelphia, Saunders, 1949, p. 559.
4. Contardo, R.: Evolution of the collagen diseases. Arch. Ophth., **56**:568, 1956.
5. Edstroem, G., and Oesterlind, G.: A case of nodular rheumatic episcleritis. Acta ophth., **26**:1, 1948.
6. Van Der Hoeve, J.: Scleromalacia perforans. Arch. Ophth., **11**:111, 1934.
7. Verhoeff, F. H., King, M. J.: Scleromalacia perforans. Arch. ophth., **20**:1013, 1938.
8. Wolter, J. R., and Landis, C. B.: Zur Klinik und Pathologie des massiven Granuloms der Sklera. Klin. Monatsbl. f. Augenh., **132**:59, 1958.
9. Petrohelos, M. A., and Wolter, J. R.: Necroscleritis nodosa. Arch. Ophth., **55**:221, 1956.

EYE PROTECTION AGAINST SMALL HIGH-SPEED MISSILES*

George M. Stewart
Army Chemical Center, Maryland

Introduction

In October, 1956, a paper dealing with the problem of eye protection against small high-speed missiles was presented at the 61st annual session of the American Academy of Ophthalmology and Otolaryngology, Chicago, Illinois.[1] It was pointed out that the prevention of penetrating ocular wounds is of primary importance since the loss of an eye drastically curtails the usefulness of man at his chosen profession. Industry and some branches of the Armed Forces presently protect the eye by heat-treated glass lenses. The use of this lens was justified by the finding that against a steel ball drop test (ASA) the heat-treated lens is unquestionably superior to the unheat-treated lens.

Research in the field of eye protection was stimulated by clinical observation[1] of perforating eye wounds which often were caused by foreign bodies which had as their largest dimension one or two mm. To penetrate the cornea or sclera such small missiles must have considerably higher velocities than larger missiles. With this thought in mind it was postulated that against small missiles at high velocities lenses could react differently at impact than for larger missiles at low velocities. Until 1953, very little work had been done with the ballistic evaluation of lenses when impacted by small missiles at high velocities because of the inability to propel small missiles at high velocity levels.

Several years ago a gun using helium as a propellant was developed which could propel missiles of various shapes and weights at both low velocities (75 ft./sec.) and relatively high velocities (1,800 ft./sec.).[2] This gun was used to evaluate lenses and rabbit eyes.

Figure 1 shows the ballistic range with

---

* From the Biophysics Division, U. S. Army Chemical Warfare Laboratories.

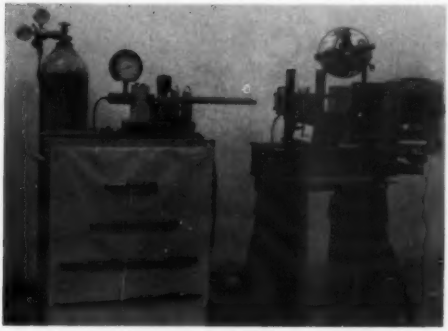


Fig. 1 (Stewart). Experimental range.

helium gun, velocity measuring screen, camera, light source and eye mounted in a gelatin block in position for a test. Figure 2 shows a velocity measuring device with a pistol and lens mounted on the jig. This velocity measuring device was one based on the accurately measured time interval between interruptions of two light beams spaced a known distance apart (in this case 10 cm.). This method was devised to avoid the uncertainty introduced into velocity measurements by more conventional means, such as breaking wires or circuits printed on paper. These uncertainties would be large for the small missiles required for this study.

To test the theory that lenses would react differently to the impact of small missiles at high velocities than to large missiles at low velocities about 3,000 lenses have been evaluated. Lenses included nonheat-treated glass, heat-treated, laminated glass and plastic (allyl casting). Lenses were in two base curves, 9.0 and 12, and three thicknesses, 2.5, 3.0 and 3.5 mm. The lens under test was mounted in rubber and an adhesive paper, separated by a one-inch air space, was placed behind the lens to determine if the missile perforated the lens or particles of the lens were thrown off the back of the lens.

When testing eyes, rabbits varying in age from five to seven months were killed by administering an intraperitoneal injection of pentobarbital sodium. The eye was removed and mounted in a gelatin block for ballistic limit evaluation (fig. 3). The tests were initiated within five minutes after the eyes were dissected from the animals, and all shots were directed toward the center of the cornea.

The missiles used in the evaluation of the lenses and eyes consisted of steel spheres, cubes and cylinders in the weight range of 3.7 mg. to 130 mg.

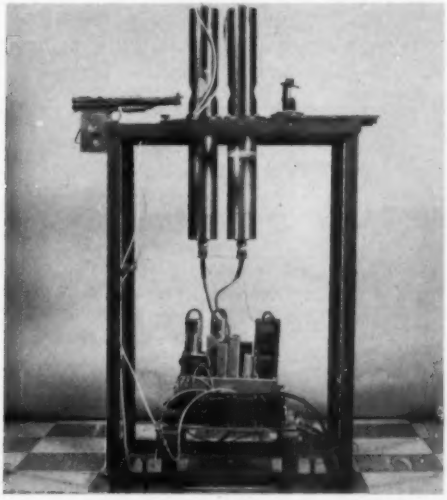


Fig. 2 (Stewart). Velocity measuring equipment.

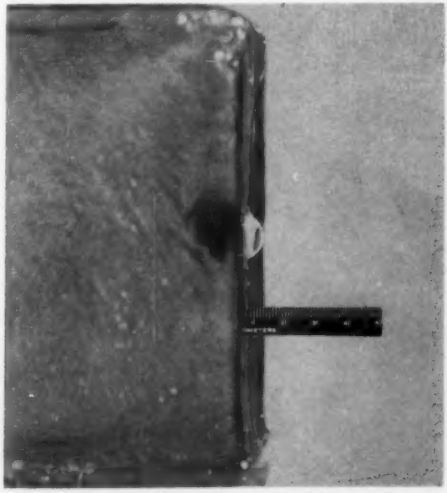


Fig. 3 (Stewart). Rabbit eye mounted in gelatin.

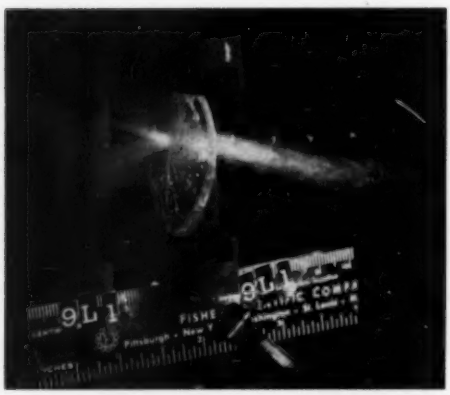


Fig. 4 (Stewart). Impacted lens, showing secondary missiles.

Discussion

To establish a ballistic limit for a lens or eye enough rounds of the sphere, cubes or cylinder were fired to obtain at least one partial and one complete penetration. A complete penetration of a lens is considered to occur when the impacting missile causes glass to be thrown from the back of the lens or the missile perforates the lens (fig. 4). A complete penetration of a rabbit eye occurs when the impacting missile punctures the cornea (fig. 5) permitting loss of the aqueous humor. A missile impact that fails to develop a complete penetration is considered a partial penetration. A ballistic limit is determined by plotting the partial and complete penetrations (fig. 6) and by averaging from one to 10 of the highest velocities resulting in partial penetration with an equal number of the lowest velocities resulting in complete penetration.

Table 1 lists the ballistic limit of the lenses tested. Included in this table also are the ballistic limits for the lenses that were reported in the first paper. (Those ballistic limits in Table 1 that differ from the results previously reported are due to a change in the definition of a complete penetration. In the first work[1] a complete penetration was defined as a condition where the lens cracked or was perforated by the missile.) Ballistic limit results from this table show that the nonheat-treated glass lens is superior by 270 percent over the heat-treated glass lens when impacted by a 1.0-mm steel sphere. Both of these lenses, however, are inferior in the protection offered when compared to the laminated lens or the plastic lens. During test it was noted that both of the glass lenses broke partially into sharp triangular pieces or very small sharp pointed splinters. Although it was expected that the nonheat-treated glass lens would break in such a manner the findings were contrary to claims made for the heat-treated lens. Figure 7 portrays an eye that is splattered with fine pieces of glass thrown from the back side

Fig. 5 (Stewart). Expulsion of aqueous humor from impacted rabbit eye.

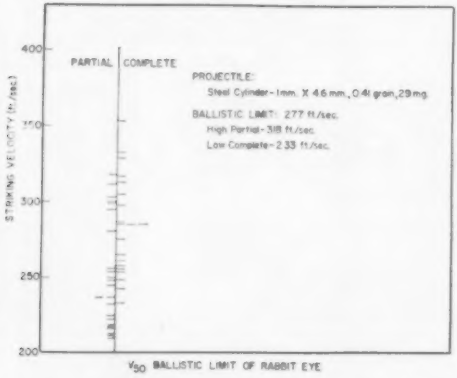


Fig. 6 (Stewart). Method of plotting and determination of V50 ballistic limit.

TABLE 1

BALLISTIC LIMITS FOR PROTECTIVE LENSES IN FEET PER SECOND

	Missile	Base Curve Nine-Diopter Thickness of Lens			Base Curve 12-Diopter Thickness of Lens		
		2.5 mm.	3.0 mm.	3.5 mm.	2.5 mm.	3.0 mm.	3.5 mm.
Heat-treated Glass	1	345	383	317	336	321	355
	2	—	147	198	139	155	142
	3	—	139	—	—	—	—
	4	468	—	562	545	—	—
Nonheat-treated Glass	1	970	—	—	925	—	—
	2	153	171	187	101	112	159
	3	—	82	—	—	—	—
	4	—	449	450	—	—	—
	5	—	391	—	—	—	—
Laminated glass	1	—	—	—	1386	—	—
	2	329	286	—	312	317	357
Plastic CR-39	1	>1600	—	—	—	—	—
	2	593	722	705	572	677	890
	3	—	—	434	—	—	—
	4	625	—	903	—	—	—
	6	313	—	346	—	—	—

1. Sphere, steel 1.0 mm., 0.040 inch, 3.7 mg., 0.057 gr.
2. Sphere, steel 2.36 mm., 0.093 inch, 53 mg., 0.85 gr.
3. Sphere, steel 3.20 mm., 0.125 inch, 129 mg., 2.01 gr.
4. Cylinder, steel 0.040 inch by 0.182 inch, 27.01 mg., 0.417 gr.
5. Cylinder, steel 0.040 inch by 0.363 inch, 54.0 mg., 0.833 gr.
6. Cylinder, steel 0.093 inch by 0.151 inch, 130 mg., 3.01 gr.

of a heat-treated lens that rejected the impacting missile.

When the size of the test sphere is increased from 1.0 mm. to 2.36 mm. the heat-treated lens offers approximately the same protection as does the nonheat-treated lens. As the weight of the steel sphere is increased the heat treated lens offers more protection than does the nonheat-treated lens.

Figures 8, 9, and 10 show the four types of lenses after being impacted by the 1.0 mm. and the 2.36 mm. steel sphere. Against the 1.0 mm. sphere at a velocity level of 422 ± 5.0 ft./sec. (fig. 8) the heat-treated lens was the only one in which a complete penetration resulted. Although the missile was

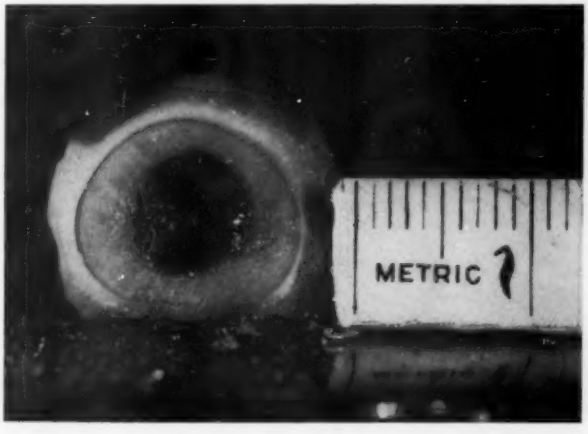
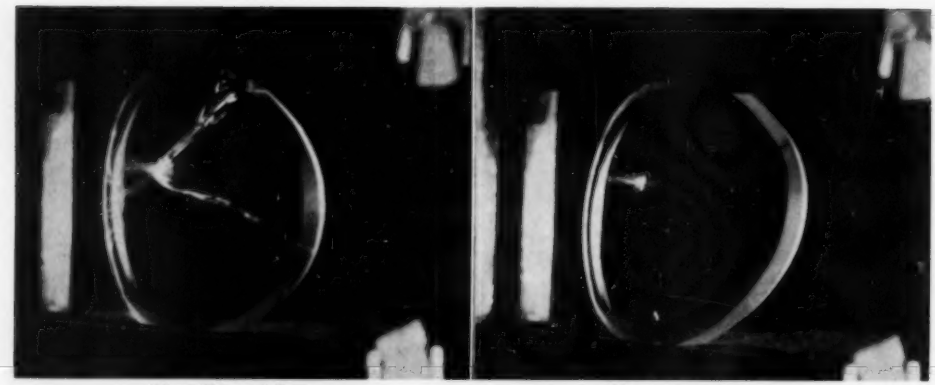
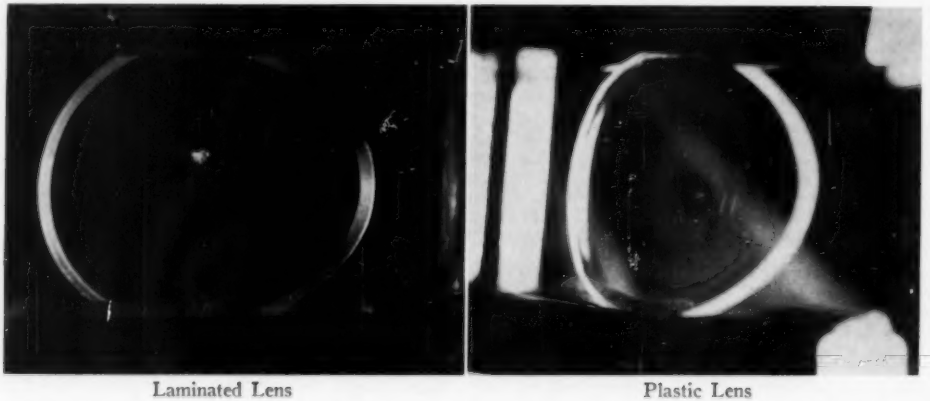


Fig. 7 (Stewart). Rabbit eye with glass splinters from broken heat-treated lens which repelled impacting missile.



Heat-Treated Lens Nonheat-Treated Lens



Laminated Lens Plastic Lens

Fig. 8 (Stewart). Lenses: 12 diopter, 0.3-mm. thick impacted by 1.0-mm. 0.057-gr. sphere at 422±5.0 ft./sec.

rejected small pieces of glass were expelled from the back side of this lens.

For the 2.36-mm. sphere at a velocity level of 280 ± 4.0 ft./sec. (fig. 9) the heat-treated and the nonheat-treated lenses were defeated. With both of these lenses the missile was rejected but a considerable quantity of glass was thrown from the back side of the lens. For the laminated lens the missile was rejected and the lens was cracked but there were no secondary missiles thrown from the back side of the lens. When the plastic lens was impacted with this sphere there was no cracking of the lens or secondary missiles. The only damage to this latter lens was a 1.0 mm. dent. Upon increasing the velocity for the 2.36 mm. sphere against these two lenses (fig. 10) the laminated lens was defeated at a velocity of 437 ft./sec. and a large quantity of glass was thrown from the back side of the lens. At a velocity of 660 ft./sec. the plastic lens defeated the missile and there were no cracks or secondary missiles.

Table 2 contains the ballistic limit results for the rabbit eye against spheres, cubes and cylinders. The result of 277 ft./sec. for the 1.0-mm. diameter cylinder is higher by 37 ft./sec. than that reported in the first paper. This change is due to the refinement of the ballistic limit by incorporating the results of additional rounds fired. In comparing the results of the eye work with that of the lens work it will be noted that the eye

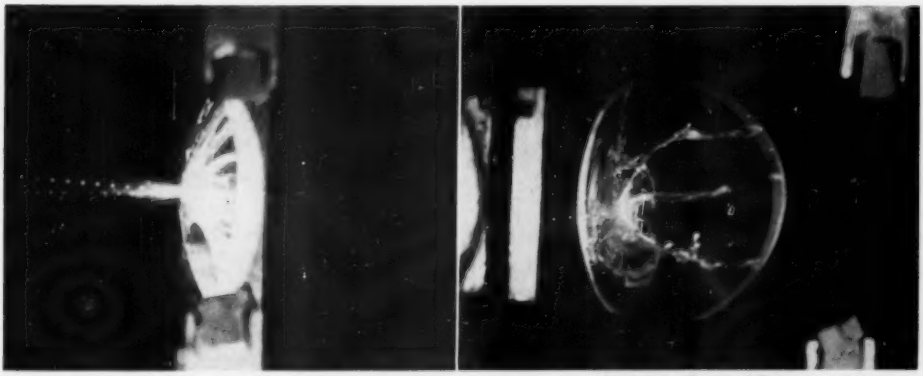
offers at least 25 percent more protection than the three thicknesses of the nine and 12 curve heat-treated lenses when impacted with the 1.0-mm. sphere. The eye, however, offers much less protection against this missile than does the laminated or plastic lens.

For the 2.36-mm. sphere the ballistic limit of the rabbit eye is at least 80 percent higher than that for the nine and 12 curve heat-treated and nonheat-treated lenses and offers at least as much protection as the laminated lens. When compared with the plastic lens the eye offers much less protection.

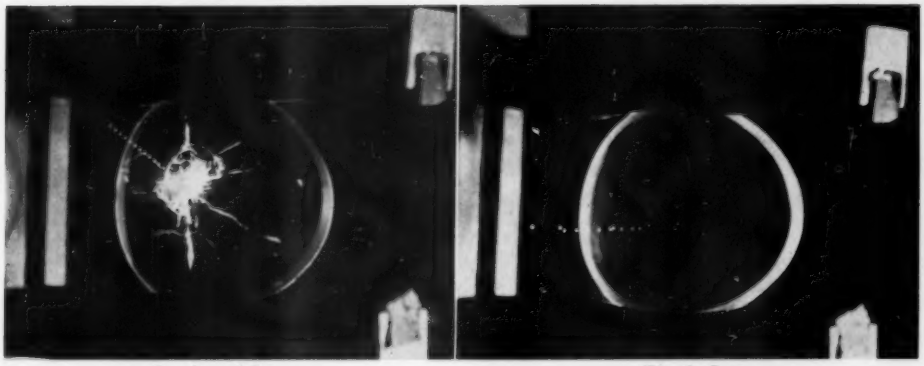
The resistance of the eye to a 3.2 mm. sphere is at least 100 percent higher than that for the one thickness of heat-treated and nonheat-treated lenses; however, as in all other comparisons the eye offers less protection (30 percent) than the plastic lens.

When changing the shape of the test missile from a 1.0-mm. sphere (0.057 gr.) to a 1.0-mm. diameter cylinder, 0.182 inches long (0.417 gr.) the eye offers much less protection than any of the lenses tested.

The results of the comparison made of the protection afforded by the eye versus the protection given by the lenses does not imply that against certain missiles at certain velocity levels one is better off not wearing protective lenses other than the plastic type. At low velocities any of the lenses will protect the eye against corneal abrasions or hemorrhages if the velocity of the missile is such that a partial penetration of the lens is obtained. The findings do imply, however, that at a velocity level where a complete

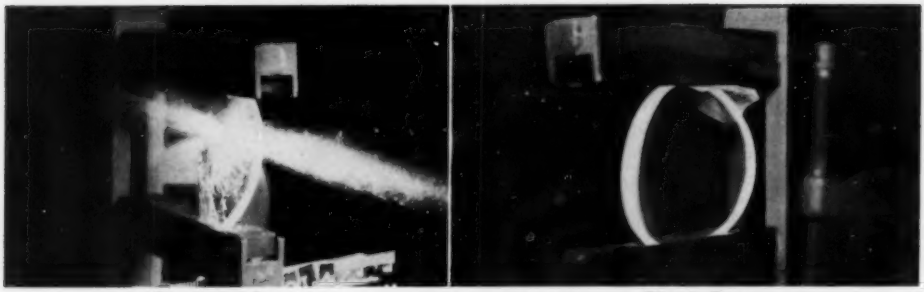


Heat-Treated Lens | Nonheat-Treated Lens



Laminated Lens | Plastic Lens

Fig. 9 (Stewart). Lenses: 12 diopter, 3.0-mm. thick, impacted by 2.36-mm., 0.85-gr. sphere at 280±4.0 ft./sec.



Laminated Lens
437 ft./sec.

Plastic Lens
660 ft./sec.

Fig. 10 (Stewart). Lens: Nine diopter, impacted by 2.36-mm., 0.85-gr. sphere.

penetration of a lens is obtained the lens can become a hazard due to secondary missiles. This is especially true for the heat-treated lens against the 1.0-mm. sphere since it breaks at a velocity lower than the ballistic limit of the eye.

It will also be noticed from the values in Table 2 that the ballistic limit of the eye is not very sensitive to the weight of the missile. For example the 2.01-gr. and 16-gr. sphere differ in weight by a factor of 8.0, yet the ballistic limits differ by a factor of approximately 2. This is also true for the 2.1-gr. and 16-gr. cube. For missiles of similar geometry there is usually a gradual decrease in ballistic limit as missile weight increases, but there is an exception even to this in that the ballistic limit against the 225-gr. cube is slightly higher than against the 64-gr. cube. During the ballistic limit tests of the eye it was noted that many of the cubes fired made flat hits against the cornea; and therefore, as the missile weight increased the area presented to the eye increased. Because of this increase in presented area more of the kinetic energy of the impacting cube is believed to be utilized in deforming the eye.

Cubes striking at velocities near the ballistic limit are frequently rejected even after penetrating the cornea or sclera. When spheres hit the eye at velocities near the ballistic limit and a complete penetration results, the sphere is often retained in the anterior chamber (fig. 11).

Summary

From the foregoing discussions and results it is suggested that, under those working conditions where one may be subjected to impacts of very small missiles, less than 2.0-mm. diameter, protective lenses be utilized that are made of either plastic, laminated or nonheat-treated glass. For the greatest over-all protection of the eyes, plastic lenses would seem to be the first choice.

There are many advantages to plastic lens spectacles other than their offering the best protection against impacting missiles. Balding[3] points out, as do plastic lens manufacturers, that plastic lenses can be manufac-

TABLE 2

Ballistic limits for rabbit eye in feet per second

Spheres				Cylinder	Cubes				
1.0 mm. 0.057 gr.	2.36 mm. 0.85 gr.	3.2 mm. 2.01 gr.	6.4 mm. 16 gr.	1.0 Diameter 0.417 gr.	2.1 gr.	4.2 gr.	16 gr.	64 gr.	225 gr.
475	350	325	152	277	205	123	119	73	93

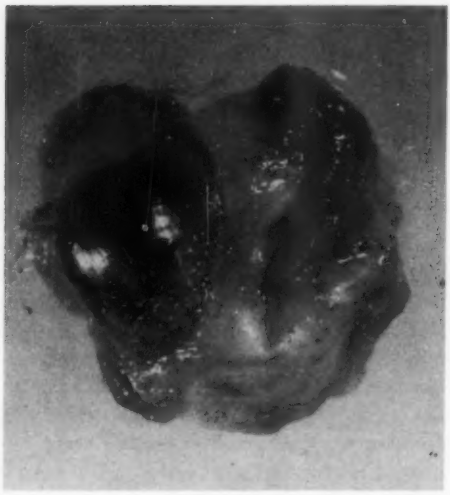


Fig. 11 (Stewart). Sphere: 0.250 inches, 16 gr., retained in anterior chamber of eye.

tured which are about 50 percent lighter in weight than glass lenses, are as clear as the finest glass and their resistance to misting is much greater than glass. If absorption is a requirement, color can be added to plastic lenses much more uniformly and there is no increase in weight as there is with glass. Plastic lenses can be made into single vision and bifocal powers.

There are two principal disadvantages to plastic lenses, first their greater cost and second their susceptibility to scratching; however, these are primarily economic rather than physical disadvantages. Plastic lenses are being manufactured today that offer high resistance to abrasives and with proper care should last for the duration of the prescription. Plastic lens spectacles can be furnished with side shields that can be instantly attached or detached without the use of tools.

Biophysics Division.

ACKNOWLEDGMENT

I am greatly indebted to Dr. H. W. Rose of the School of Aviation Medicine, USAF, Randolph Field, Texas, for his interest in this study, valuable advice, technical assistance, and supplying lenses; to Dr. Elmer G. Worthley, Biophysics Division, for his comments and stimulating discussions; to Dave Grossman, Army Chemical Center, Maryland, for the design of optical baseline; and to Maryan Lewis for her technical assistance.

REFERENCES

1. Rose, H. W., and Stewart, G. M.: Eye protection against small high-speed missiles. Tr. Am. Acad. Ophth., May-June, 1957, pp. 404-409.
2. Stewart, G. M.: Chemical Warfare Laboratories Report (CWLR) 2046, Army Chemical Center (Nov.) 1957.
3. Balding, G., and Balding, W.: EENT Monthly, Nov. 1954, p. 33.

THE LOCALIZATION OF DIAMOX-S^{35} IN THE RABBIT EYE*

SEYMOUR B. GOREN, M.D., FRANK W. NEWELL, M.D., AND JOHN J. O'TOOLE, M.D.
Chicago, Illinois

The primary action of acetazolamide (Diamox, Lederle) is the inhibition of the enzyme carbonic anhydrase which catalyzes the reversible hydration of carbon dioxide. Although a general systemic effect may contribute to the decreased intraocular pressure observed after the administration of the drug, it has been thought that Diamox acts primarily as a direct inhibitor of the enzymatic reactions in the ciliary processes.[1-8] Since Diamox is not metabolized in the body and is excreted unchanged in the urine,[9-13]

* From the Department of Surgery (Ophthalmology), The University of Chicago. This investigation was supported in part by a research grant from the National Society for the Prevention of Blindness and by Research Grant Number B-1515 from the National Institute of Neurological Diseases and Blindness.

We are indebted to Mr. H. Lal for technical aid received in this study.

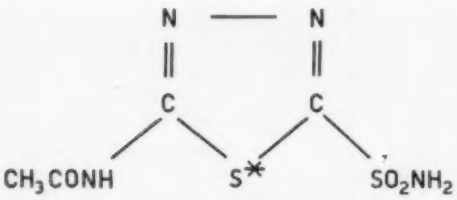


Fig. 1 (Goren, Newell and O'Toole). Formula of acetazolamide showing the position of the radioisotopic label.

the possibility of breakdown products causing the observed physiologic responses has been dismissed. The purpose of this study was to investigate the localization and metabolism of acetazolamide in the rabbit eye by means of Diamox labelled with radioactive sulfur.

Technique

Diamox-S^{35} was synthesized by the method developed by Clark and Roth[14] using S^{35} as a substrate. The specific activity of the compound was 82 mc. per mg. The position of the radioisotopic label in the azole ring of the molecule is shown in Figure 1. Chromatograms were made in both butanol-water and methyl-ethyl-ketone-water systems in order to assure the radioactive purity of the drug used. Chromatograms were repeated immediately before and after all animal studies to exclude decomposition of the compound into other radioactive substances.

Male albino rabbits weighing 2.15 to 2.35 kg. were given a single dose of one mc. per kg. of body weight of acetazolamide-S^{35} into the marginal vein of the ear. The carrier Diamox amounted to 12.2 mg. per kg. of body weight. Two hours after the administration of the labelled acetazolamide, 20 mg. of heparin was given intravenously and the animal was anesthetized with pentobarbital sodium. The chest was then opened and the aorta cannulated through the left ventricle. The right ventricle was incised, the inferior great vessels clamped off, and the rabbit perfused with 2,000 cc. of human plasma containing 0.375 mg. per cc. of nonradioactive Diamox. The perfusion was started within three minutes and completed within 20 minutes after the initial incision was made. The use of human plasma as the perfusing medium rather than normal saline was the chief modification of the technique described by Roth, Schoolar, and Barlow in their studies of the localization of acetazolamide in the brain.[15–17] Following the perfusion, the eyes were quickly enucleated and placed into a beaker of isopentane suspended in a Dewar flask of liquid nitrogen. After freezing, the eyes were transferred directly to a freeze-dry apparatus. They remained in the freeze-dryer at −20°C. at 0.001 to 0.003 mm. Hg for five days at which time they were imbedded in paraffin in vacuo.

Sections one and three microns thick were cut with the sliding microtome. No liquid was used in the process. In order to obtain whole sections and to facilitate direct transfer of the sections to autoradiographic plates, cellophane adhesive tape was placed on top of the paraffin block before each section was cut.[18] In this manner, each section

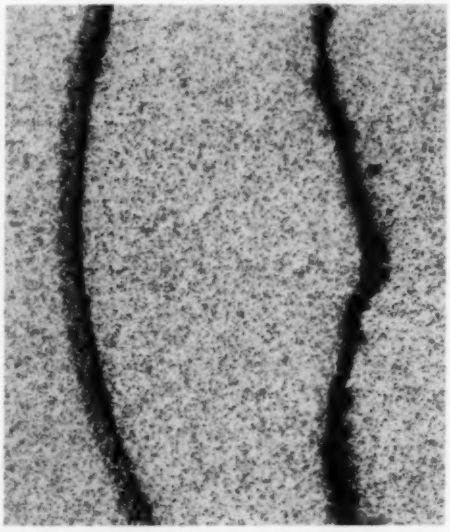


Fig. 2 (Goren, Newell and O'Toole). Autoradiograph showing the relatively high concentration of Diamox-S^{35} in the iris. Note the accumulation of the radioisotope in the inner layers of the cornea.

had a "backing" which held the tissue intact so that the specimen could be easily handled.

Autoradiographs were made using both Kodak No-Screen X-ray film and NTB-2 (5.0 micron thickness) emulsion plates. The sections were either placed directly onto the photographic plates or caused to adhere to it by means of a thin layer of egg albumin. Following exposure of the plates, the adhesive backing of the sections were floated off in xylol, the autoradiograms developed, and the tissues stained with hematoxylin and eosin.

The transfer of Diamox into the eye was studied by means of paracenteses of the anterior chamber aqueous humor or vitreous humor. Paracenteses were performed in various animals both before and after perfusion, and the ocular fluids obtained were analyzed for radioactivity. Chromatograms were also made of the extracts of the entire homogenized eye to assure that the radioactive sulfur was still incorporated into the acetazolamide molecule and not into breakdown substances.

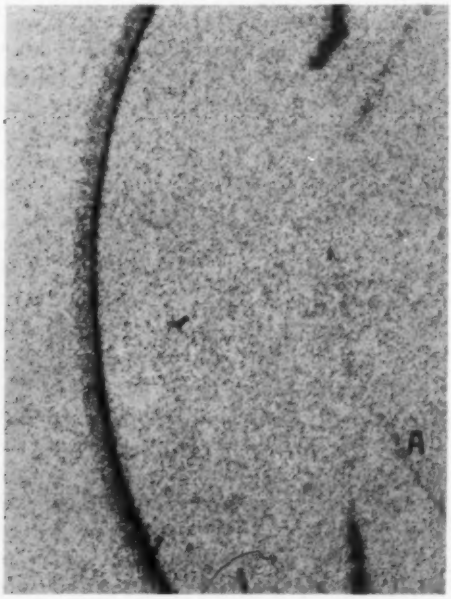


Fig. 3 (Goren, Newell and O'Toole). Autoradiogram showing the paucity of the radioisotope which has been incorporated into the lens. The lens (A) is seen as a light convex surface.

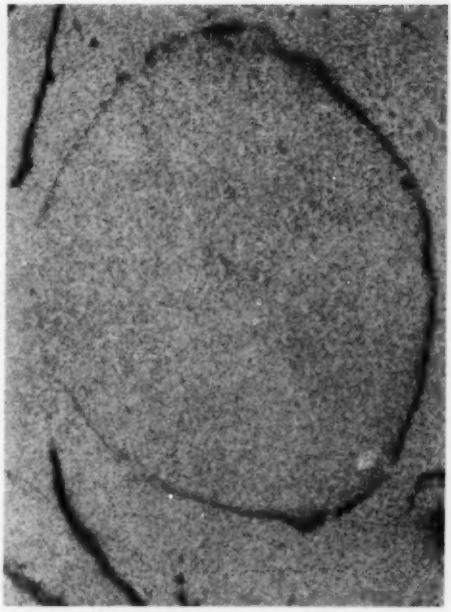


Fig. 4 (Goren, Newell and O'Toole). Autoradiogram demonstrating the localization of Diamox-S^{35} in the lens. The plate has been overexposed so that the lens may be studied. During processing, the lens tumbled so that the surface which appears to be posterior in the photograph is actually anterior. Note that the anterior surface contains more Diamox-S^{35} than the posterior. The iris is shown for orientation.

Results

The ciliary processes, iris, and inner layers of the retina were found to have the highest concentrations of Diamox. The next greatest concentrations on the autoradiograms were in the corneal endothelium and Descemet's membrane. The sclera contained moderate amounts of Diamox, less than the above-mentioned heavily impregnated tissues but more than the corneal stroma and epithelium. Very little Diamox was found in the lens and only with overexposure of the plates could an autoradiographic image of the lens be seen. More Diamox concentrated on the an-

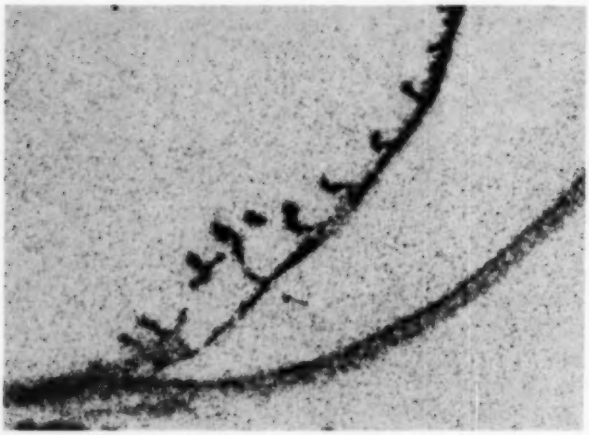


Fig. 5 (Goren, Newell and O'Toole). Autoradiograph of an oblique section through the angle demonstrating the relatively high concentration of Diamox-S^{35} in the ciliary processes and iris as compared with the surrounding structures.

terior surface of the lens than on the posterior surface with the transition from darker to lighter areas taking place in the vicinity of the equator. Minimal quantities of Diamox were found in the choroid. The level here was difficult to determine because of the marked shrinkage of the posterior uveal tract during freezing and dehydration. As can be seen from Figure 6A, the perfusion removed the blood from the ocular tissues, and erythrocytes were not seen in even very small vessels.

Chromatograms of anterior chamber aqueous humor and vitreous humor, immediately before and after perfusion, revealed no Diamox-S^{35} to be present, and no significant amounts of radioactivity was found in these fluids with the flow counter.

Chromatograms of the extracts from the whole homogenized eye revealed no difference from the pure control Diamox-S^{35}; that is, all had only one band of the same magnitude, whether or not the eye had been perfused. Therefore, it may be assumed that Diamox is not metabolized in the eye.

Discussion

A discussion of the localization and metabolism of Diamox-S^{35} in ocular tissues requires an explanation of several factors. It is evident that the autoradiograms represent unmetabolized Diamox-S^{35}, and not breakdown products because chromatographic studies demonstrate that Diamox in the eye is in an unaltered state. It is not probable that this drug reaches its final places of localization solely on the basis of random diffusion into body fluids. If this were the basic mechanism of distribution, one would expect to find moderately high amounts of radioactivity in the anterior and vitreous chambers. The absence of Diamox in the major intraocular fluids also dismisses the possibility that the localization in the inner cornea and retina is an artefact caused by the precipitation of radioactive particles in the anterior and vitreous chambers on contiguous tissues as a result of freezing and dehydration.

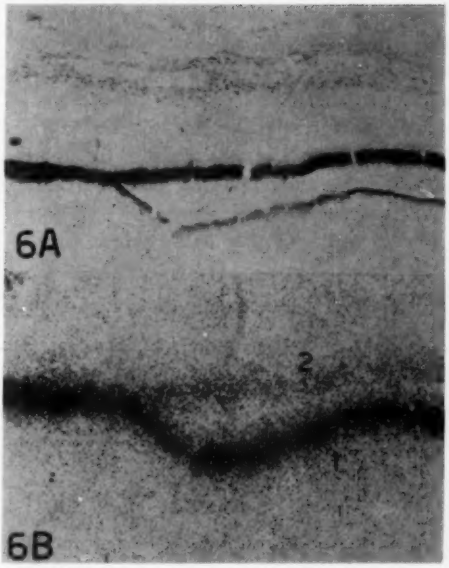
It is possible that no radioactivity was found in the ocular chambers because after two hours the Diamox which had entered the eye had been incorporated into the ocular tissues, thereby leaving the major ocular fluids free from radioactivity. Wistrand,[13] using chemical techniques, found appreciable amounts of acetazolamide to be present in the blood, anterior, posterior, and vitreous chambers two hours after the intravenous administration of the drug. However, he gave the animal either a continuous infusion of Diamox or a single injection of 100 mg.

per kg. of body weight. In the present investigation, no attempt was made to maintain steady-state conditions, and little radioactivity was present in the blood plasma two hours after the administration of the diamox-S^{35}. Therefore, the discrepancies between our results may be due to differences in the quantities of acetazolamide given.

Preliminary studies revealed that both the perfusion with plasma and the freeze-dry technique were necessary in this experiment. If normal saline solution or plasma not containing nonradioactive Diamox was used as a perfusing medium, the Diamox was leeched out of the tissues; if the eye was processed in routine water-containing solutions, the water-soluble Diamox was also lost. This water-solubility factor also prevented the use of high resolution autoradiographic stripping film in this investigation.

It is quite probable that different structures have different affinities for Diamox on the basis of weak chemical bindings between the drug and tissue.[17] This would give rise to a specific "Diamox-binding capacity" for specific tissues. This capacity for binding Diamox is probably not solely determined by the amount of carbonic anhydrase in the tissue involved. Previous workers[19] have not found a good correlation between levels of carbonic anhydrase in different areas of the cat brain and the differential uptake of Diamox in those areas. Ballintine and Maren,[3] using chemical techniques, observed no differences in carbonic anhydrase activity, or in Diamox uptake by specific ocular tissues, in rabbits which responded to the administration of Diamox with a fall in intraocular pressure as compared with those that did not. These workers also found that the amount of acetazolamide reaching the lens was not sufficient to cause any decrease in the carbonic anhydrase activity of the lens. This may be explained on the basis of such minute quantities reaching the lens as is shown in the present study.

It is felt that the localization of Diamox in the eye of the rabbit is not only dependent upon the amount of Diamox being presented to the area concerned, but also upon a preferential uptake of specific tissues with a superimposed Diamox-binding capacity of those tissues. Since there is no direct blood supply to either the cornea or the lens, and since no Diamox was found in either the anterior or vitreous chambers, there is no reason to assume that more Diamox reaches the corneal endothelium than the lens capsule. Although no posterior chamber paracenteses were performed, one would not expect an appreciable amount of Diamox-S^{35} to be present there in view of our other findings. Therefore, it is quite possible that the Diamox-binding capacity of the corneal endothelium is greater than that of the lens with a resultant difference in the amounts of Diamox localized in these structures after two hours.



Figs. 6A and 6B (Goren, Newell and O'Toole) (6A) Section of retina and choroid stained with hematoxylin-eosin. Note the artefact separation of the retina. (6B) Autoradiogram of the portion of the eye seen in (6A). The inner layers of the retina (1) are seen as a more dense area as compared with the outer layers (2).

Although very thin sections of tissues and

some extremely sensitive nuclear emulsion plates were used in this study, the very nature of S^{35}, a relatively strong beta emitter, prevented the localization of Diamox on an intracellular level. The scatter of beta rays from S^{35} precluded an analysis of cellular detail. This study is being extended, using Diamox labelled with tritium, so that intracellular structures may be localized.

Summary

By means of S^{35}-incorporated Diamox, and autoradiographic and chromatographic techniques, the localization and metabolism of Diamox in the rabbit eye have been studied. The findings are as follows:

1. The ciliary processes, iris, and inner layers of the retina were found to have the highest concentrations of Diamox.

2. Moderate amounts of Diamox were localized in the corneal endothelium and Descemet's membrane.

3. The sclera, corneal stroma, and corneal epithelium contained small amounts of Diamox.

4. Very little Diamox was present in the lens, overexposure of the autoradiograms having been necessary in order to visualize it.

5. Minimal amounts of Diamox were found in the choroid. The level here was difficult to determine because of the marked shrinkage of the posterior uveal tract during freezing and dehydration.

6. No Diamox was found in the anterior chamber aqueous humor or in the vitreous humor two hours after the intravenous administration of 12.2 mg. per kg. of body weight.

7. Diamox was present in the eye in an unmetabolized state.

8. It is felt that the localization of Diamox in the rabbit eye is partially dependent upon a preferential uptake of specific tissues with a superimposed Diamox-binding capacity of those tissues.

950 East 59 Street (37).

References

1. Becker, B.: Carbonic anhydrase and the formation of aqueous humor (The Friedenwald Memorial Lecture). Am. J. Ophth., **47**:342, 1959.

2. Wistrand, P. J.: Carbonic anhydrase in the anterior uvea of the rabbit. Acta Physiol. Scandinav., **24**:144, 1951.

3. Ballintine, E. J., and Maren, T. H.: Carbonic anhydrase activity and the distribution of Diamox in the rabbit eye. Am. J. Ophth., **40**:148, 1955.

4. Green, H., Capper, S. A., Bocher, C. A., and Leopold, I. H.: Effect of acetazolamide (Diamox) on carbonic anhydrase activity of anterior uvea of the rabbit eye. AMA Arch. Ophth., **52**:758, 1954.

5. Becker, B.: The mechanism of the fall in intraocular pressure induced by the carbonic anhydrase inhibitor, Diamox. Am. J. Ophth., **39**:177, 1955.

6. ———: Chemical composition of human aqueous humor: Effects of acetazolamide. AMA Arch. Ophth., **57**:793, 1957.

7. Maren, T. H.: Carbonic anhydrase inhibition in the elasmobranch: Effect on aqueous humor and cerebrospinal fluid CO_2. Fed. Proc., **17**:391, 1958.

8. Wistrand, P. J.: Local action of the carbonic anhydrase inhibitor, acetazolamide, on the intraocular pressure in cats. Acta Pharmacol. & Toxicol., **14**:27, 1957.

9. Maren, T. H., Mayer, E., and Wadsworth, B. C.: Carbonic anhydrase inhibition: I. The pharmacology of Diamox 2-acetyl-amino-1,3,4-thiadiazole-5-sulfonamide. Bull. Johns Hopkins Hosp., **95**:199, 1954.

10. Schoolar, J. C.: Studies on the localization of urea-C^{14}, acetazoleamide-S^{35} and isonicotinic acid hydrazide-C^{14} in specific areas of the cat brain. Thesis, University of Chicago, 1957.

11. Achor, L. B., and Roth, L. J.: Metabolic fate of acetazoleamide S^{35} (Diamox) in the cat. Fed. Proc., **16**:277, 1957.

12. Maren, T. H., and Robinson, B.: The pharmacology of acetazolamide as related to cerebrospinal fluid and the treatment of hydrocephalus. Bull. Johns Hopkins Hosp., **106**:1, 1960.

13. Wistrand, P.: The effect of carbonic anhydrase inhibitor on intra-ocular pressure with observations on the pharmacology of acetazolamide in the rabbit. Acta Pharmacol. & Toxicol., **16**:171, 1959.

14. Clark, L., and Roth, L. J.: The synthesis of 1-S^{35}-Diamox. J. Am. Pharm. A., **46**:646, 1957.

15. Schoolar, J., Barlow, C., and Roth, L. J.: Autoradiography of carbon-14 labeled isoniazid in brain. Proc. Soc. Exper. Biol. & Med., **91**:347, 1956.

16. Barlow, C., Schoolar, J., and Roth, L. J.: Distribution of carbon-14 labeled isoniazid in brain. Neurology, **7**:820, 1957.
17. Roth, L. J., Schoolar, J., and Barlow, C.: Sulfur^{35}-labeled acetazolamide in cat brain. J. Pharmacol. & Exper. Therap., **125**:128, 1959.
18. Palmgren, A.: Tape for microsectioning of very large, hard or brittle specimens. Nature, **174**:46, 1954.
19. Ashby, W., Garzoli, R. F., and Schuster, E. M.: Relative distribution patterns of three brain enzymes, carbonic anhydrase, choline esterase, and acetyl phosphatase. Am. J. Physiol., **170**:116, 1952.

A HISTORY OF PHILIPPINE OPHTHALMOLOGY*

GEMINIANO DE OCAMPO, M.D.
Manila, Philippines

"Ang di marunong lumiñgon sa pinanggaliñgan ay di makararating sa paroonan."† He who does not know his past will not reach his goal. This Filipino native saying stresses the importance of knowing history and the past in order to arrive at one's goal in the future. This is my theme and I shall try to trace the history of Philippine ophthalmology so that the Philippine Ophthalmological Society will know and visualize whither it is going.

A sense of history is often more important than a knowledge of history. The details of history arouse in us that sense of history which remains a force after the details are forgotten. The details of the history of Philippine ophthalmology that I shall relate may be incomplete but I hope that its lessons will be long lasting.

The history of Philippine ophthalmology may be divided into three periods: the precolonial era, the colonial era, and the independence era.

PRECOLONIAL ERA

According to Bantug,[1] "the beginning of medicine in the Philippines are shrouded in the mist of time. No authentic monuments have come down to us that indicate with certainty early medical practices." It seems certain, however, that many primitive ophthalmologic practices, instruments, and beliefs in the Philippines date from before the Spaniards came to this country.

Just as the ways of life and living in prehistoric times are seen even now in some outskirts of civilization so is ophthalmologic folklore in the Philippines still observed even now in our rural areas. These medical practices were intertwined with the pagan religion, myths and superstitions. There were gods and dieties for cure and protection or for evil and the cause of diseases. During this mythical period, medical practitioners were priests or, mostly, priestesses who acted as the human media for the Spirits of Good or Evil in the treatment or prognosis of disease. According to Bantug,[1] citing from the *Chronicler of Legaspi:* "The priestess wears a wig of golden hair, a diadem on her head and in her hand she holds a straw fan and a bamboo stick." According to Loarca,[1] the priestesses dressed very elegantly with garlands on their heads and glittered with gold and jewels. The ceremonies of healing consisted of invocation and offerings. The eye diseases at this period must have been treated like any other diseases.

In addition to the pagan priestesses who cured diseases through the Spirits, there were "curanderos."‡ These were men who were born with or possessed special healing powers. The "herbolarios,"§ who today are called "quack doctors," dealt with general

* Read at the Inaugural Meeting of the Philippine Ophthalmological Society, December 12, 1958.
† A Tagalog proverb.
‡ Healers.
§ Herb healers.

medicine but some of them seemed to have treated only, or also, eye diseases. These were called "mangkakahig,"* "magkakakay," or "magbubulo."

The most common, if not the only ophthalmic surgical procedure, that has come down to the present from this era is the "kahig." Even now this is a common practice in the rural areas and some famous "magkakahig," such as the one in Bocaue, Bulacan, are said to have lucrative ophthalmologic practices and a large clientele of rural eye patients.

"Kahig" means "scrape" and it seems that it is done for any actual or imaginary whitish area or spot in the cornea, conjunctiva, or deeper structures. It is commonly done for real or imagined foreign bodies or insect hairs, corneal ulcers, or phlyctenules.

There are many appliances or ophthalmic instruments used for this "kahig." They are the "kampit" or small bolo, needles, plant "spines," paraffin which has been molded with pointed ends, and other sharp objects. Some even use the edge of coins. The appliances being unsterile, infections often occur; hence some corneal ulcers may even be aggravated but it seems that barring sterility, the principle of "kahig" to remove necrotic tissue in corneal ulcers is a sound surgical concept.

Other ophthalmologic folklore and practices of this era that have come down to us may be mentioned. Second sight in old age, as nearsightedness due to cataract, is welcomed by many, not knowing its later stages. Congenital anomalies like ptosis, slit palpebral aperture, or even squinting are blamed on the conceiving mother looking at or getting fond of dolls or other objects or persons having such ocular appearances. "Ang duling ay dalawa ang tiñgin."† The squints have double vision or "Duling, walang gawang magaling."‡ The squints do nothing good. Some consider paralytic squints as due to "kulam" (evil spirits) or "hañging libot" wandering humors in the body.

Most blindness occurring in advanced age is attributed to old age and since it is considered "talaga ng Dios" or the will of God, nothing is done about it. In fact one of the present causes of blindness and an enemy of the fight against blindness in this country is this Filipino fatalism.

There are several primitive ocular preparations in the rural areas. Urine is used as an eyewash for "sore eyes" or conjunctivitis. Human milk is a common external eye medication for many eye diseases. We now know that human milk not only contains antibodies but also corticosteroids and probably other soothing substances and that it may be not only anti-inflammatory but also mildly antiseptic. Sampaguita‖ water which is made by soaking sampaguita flowers in a glass of water overnight is used in some places for aromatic eyewash.

Colonial era

Spanish occupation:

The Spaniards converted most of the Filipinos to christianity, so the mystic physician priestesses called "Katalonan," according to Blumentritt, had to give way to the Spanish missionaries, some of whom recorded medical practices of the time. In 1708, Father Pablo Clain finished his work entitled, *Remedios Faciles para Diferentes Enfermedades.* This was published in 1712. One chapter, according to Bantug,[1] contained "modes de preparar algunas medicinas" and among those mentioned was "Colirios" or collyria. One of the most frequent causes of blindness in the Philippines during this time was smallpox which caused corneal ulcers and all sorts of complicated leukomas, or "pilak" in Tagalog. The earliest recorded epidemic of smallpox in the Philippines was reported by P. Chirino as in 1591.

The curanderos, herbolarios, and magkakahigs of the precolonial era continued to

* Scrapers.
† A Tagalog saying.
‡ Another Tagalog saying.

‖ A national flower of the Philippines.

treat eye diseases, although in the 18th and especially the 19th centuries, when ophthalmology flourished in Europe,[2, 12] some European (Spanish, English, and French) ophthalmologists must have found their way into this country and practiced ophthalmology here. One such report, "Twenty years in the Philippines," is by Paul P. de la Gironiere,[3] a French naval surgeon who studied at the Hotel-Dieu of Nantes. He arrived in Cavity in May, 1820, being the only physician in the place at that time, although he mentions Indian or native sorcerers or mystics. He transferred to Manila after his boat left. The hospital in the Walled City of which he writes must have been San Juan de Dios Hospital, founded in 1577 and passing to the administration of the Hermandad de la Miscericordia in 1696.

Gironiere relates how he removed the eye of a Spanish Captain, Don Juan Poras, which was afflicted with tumor. In order not to wait 18 months for an artificial eye from Paris Gironiere had to make one from some pieces of glass and a tube, with the help of a carriage painter and a jeweler. This gave him fame as "Señor Don Pablo, the eminent French physician—most especially the clever oculist." He continues his narrative:

"Notwithstanding my youth and inexperience, my first success gave me much confidence that I performed several operations upon persons afflicted with cataracts, which succeeded most fortunately."

This must have been around two years after he arrived in Manila, about 1822, and could be the first cataract operation performed in the Philippines by a French surgeon, who also practiced general medicine. At least I can find no earlier case on record. Señor Don Pablo was also appointed surgeon-major of the first light regiment. He later married a Spanish widow, bought the hacienda Jala-Jala and gave up the practice of medicine. He returned to France in 1839 after his wife and son died.

About this time, as Bantug[1] states, "to study medicine it was necessary to go to Mexico at great expense because of the long journey. Moreover there were but few physicians coming from the mother country." Nicolas-Fernando[10] mentioned, "In Manila, during the last years of the Spanish regime, there were two Spanish physicians, Drs. Biola and M. C. Tornell who were also practicing oculists." But it is not true as Nicolas-Fernando[10] states that "Rizal is known to have performed the first cataract extraction in these islands as early as 1887" because Gironiere performed cataract extraction 50 years earlier in 1822.

Bantug[1] reports from the "Estadistica Operatoria de las Salas de Cirugia de Hombres y Mujeres del hospital Civil de San Juan de Dios" that in 1875 there was one cataract extraction and in 1876 there were two. Even when Rizal was in Europe studying medicine and specializing in ophthalmology in 1884-1887, according to Dr. Leoncio Lopez-Rizal,[10] he received a letter from one of his relatives in Calamba stating that he was being treated by a certain Spanish oculist for his eye ailment.

On July 16, 1885, Paciano* wrote Rizal,[7] "You said in your previous letter that you intend to go to Germany to take up ophthalmology. Now you say you are going to England. You can do as you choose because this specialty would be useful to the family and in this country few or none practice this specialty."

Palma wrote,[7] "Among the masses, the news spread that a doctor Uliman (German) had arrived who was giving sight to the blind. A rustic who desired to know the doctor Uliman went to see him in his house and supposed him to be a blonde with a long beard. But when he saw Rizal who looked like any other Filipino, he exclaimed, 'Only that' and left disappointed." This illustrates our colonial mentality in ophthalmology at that time—a colonial mentality which still lingers up to the present.

There are some interesting documents presented by Bantug, regarding ophthalmol-

* Brother of Rizal, national hero of the Philippines, who was an ophthalmologist.

ogy in the later part of the Spanish era. Although the University of St. Tomas was founded in the 16th century, the college of medicine of St. Tomas was founded only in 1871, or 37 years before the University of the Philippines, College of Medicine. The late Dr. Proceso Gabriel,[1] stated that in 1876-1877, 33 students matriculated. Among the subjects given in the fourth year were surgical pathology and surgical clinics, surgical anatomy, operations and bandaging, *ophthalmology and clinical ophthalmology*, therapeutics, materia medica, and art of prescription. However, in 1889-1890, or 13 years later, ophthalmology does not appear in the fourth or any other year as a separate subject. Dr. Bantug thinks that a Spanish ophthalmologist was present when the college was established but that he probably died or went back to Spain after a few years and in 1889-1890 there was no one to present ophthalmology as a separate subject. As a matter of fact, as late as 1908, the Fr. Rector Raymundo Velasquez, O.P., in a report presented to the Faculty mentioned:[1] "In San Juan de Dios, where clinics are taught there was established during the last school year a public dispensary with departments of surgery, medicine, gynecology, pediatrics, ophthalmology and dentistry."

During the latter part of the Spanish era, several Filipino physicians took postgraduate courses in ophthalmology in European centers. Among them was Dr. Jose Rizal. Another, 10 years older than Rizal, was Dr. Joaquin Gonzales, the first president of the University of the First Philippine Republic and the father of the late President Bienvenido Gonzales. However, Rizal is believed to be the first known Filipino ophthalmologist at the end of the Spanish era.

Although he was by training and preference an ophthalmic surgeon and gained fame and fortune as an ophthalmologist, Rizal had to practice some general medicine especially during his exile in Dapitan. I have done some historical research on Rizal as an ophthalmologist and ophthalmic surgeon and have dealt lengthily on many aspects of his ophthalmological career in two papers, "Dr. Rizal, ophthalmic surgeon,"[7] and "Rizaliana on cataract."[8] The only regrettable thing is that he did not write or leave to us any scientific article in ophthalmology. His professors in ophthalmology were among the best in Europe at that time (1885-1887)—L. de Wecker, Otto Becker, Schweiger, Zulzer, and Galezowsky. I cannot find any original document that he ever studied under Ernst Fuchs, although he must have spent a few days in his clinic in Vienna before his first voyage home in 1887.

The practice, the teaching, the instruments, the prescriptions, and other phases of ophthalmology in Europe and in the Philippines at that time are all illustrated in "Rizaliana in ophthalmology," an exhibit which I presented at the Golden Jubilee Rizaliana[13] of the University of the Philippines in June, 1958.

American era

According to Nicolas-Fernando,[10] "in the early years of the American occupation, a Polish physician by the name of Lankowsky practiced as an oculist here." In these early years of the 20th century, most of those who practiced ophthalmology in the Philippines were American physicians with the United States Army. Among those who contributed to the literature were: C. J. Minor, "Glaucoma among Friars," P. G. Wolley, "Sarcoma of the ciliary body" in 1905; H. H. Rutherford, "Traumatic cataract, detached retina, and neuroretinitis," W. P. Chamberlain, "Koch-Weeks' conjunctivitis." Other Americans who came later and practiced some ophthalmology in the Philippines are E. N. Stafford, M. N. Salleby, and Waterous who seems to be still active.

Then came the Filipinos. To quote from Nicolas-Fernando,[10] "It was only in 1905 when Dr. S. B. Alberto arrived from Europe after a two-year training course in

ophthalmology at the University of Paris that ophthalmic practice may be said to have been taken up by a Filipino for the second time. At about the same time Dr. Simeon Villa, who studied in Japan, had a short-lived practice here as an oculist."

In 1911 the Department of Eye, Ear, Nose and Throat of the Philippine General Hospital was organized with Dr. Reinhart Rembe, a German (naturalized American), as its first head and professor. Thus began in the Philippines under American influence, the inclusion of ear, nose and throat with the specialty of ophthalmology, a bond which will take almost half a century to break and to free ophthalmology from the hold of otolaryngology. As if to follow the American practice of combining ophthalmology with otolaryngology the Department of Ophthalmology of San Juan de Dios Hospital was reorganized in 1914 to include otolaryngology under Dr. Alberto who started as an ophthalmologist but ended as an eye, ear, nose and throat man. As a matter of fact in no other place in the world but the United States, or in countries under its influence, has ophthalmology been bonded to otolaryngology.

Among the early Filipino physicians during the American era who practiced and taught both ophthalmology with otolaryngology were Drs. A. R. Ubaldo and H. Velarde, Sr., of the Philippine General Hospital, and Drs. S. B. Basa and C. Basa of San Juan de Dios Hospital. Drs. R. Ongsiako and V. Sevilla in Manila and L. Santos of Malolos were three Filipino eye, ear, nose and throat physicians who had extensive private practices but no teaching connections. Drs. Consing and Jalbuena were widely known in Iloilo while Dr. Valencia practiced in Cebu and Drs. Ochoa and Filoteo in Bacolod.

Among the Filipino eye, ear, nose and throat physicans in the first half of the American occupation may be mentioned Drs. Delfin and Esteban in St. Tomas University and Drs. Farrales, A. S. Fernando, F. Nicolas-Fernando, V. C. Alcantara and C. D. Ayuyao in the Philippine General Hospital.

In the second half of the American era, may be mentioned Drs. Dizon, Buendia, T. Ilano, Crisostomo, Maloles, Bernardo, de Ocampo, Yambao, J. N. Cruz, Peralta, Cid, Luczon, Tamesis, C. Sevilla, Nañagas from the Philippine General Hospital and Drs. E. Reyes, J. Eusebio, F. Villaroman, S. Alberto, Jr., F. Sta. Maria, E. Osmeña, G. Macatañgay and T. U. J. Herrera from the University of St. Tomas. Several of them had postgraduate training in Europe, mostly in Vienna, and a few had taken some courses in America, particularly New York.

Among the early contributions of Filipinos to Philippine Ophthalmologic literature were: Alberto, "Trachoma, its prophylaxis," in 1912, and the "Results of mixed treatment on trachoma," in 1914. Ubaldo, 1912 to 1918, the "Krönlein operation for removal of intraorbital tumors, with report of a case operated on," "Observations on amblyopia after pregnancy," and "Chronic infections of the lacrimal sac: Bacteriological examinations of 25 cases; Surgical treatment"; Dr. Velarde, "Cases of conjunctivitis vernalis in the Philippine General Hospital" in 1917 and "Six cases of glioma retinae" in 1919.

Ophthalmologic contributions from Filipino physicians during the late American era were—Velarde, "Iridectomy in the treatment of glaucoma: With report of 14 cases," in 1922, and "Corneal paracentesis" in 1920; Ubaldo, "Intracapsular cataract extraction after Barraquer's technique," in 1923.

The first erisophake in the Philippines, an early Barraquer model used by Dr. Ubaldo is now kept at the U.P. Medical History Museum. Fernando published "Causes of blindness among Filipinos as observed in the P.G.H. dispensary," in 1922, "Ocular manifestations in leprosy as observed in Culion," in 1923 and "Errors of refraction among Filipinos," in 1927; C. D. Ayuyao, "Corneal lesions in Beriberi," in 1933, and

"Clinical observations on xerophthalmia," in 1937. E. Reyes published "Blindness after sleeping with wet hair: A case of vasoconstriction of the retinal arteries," in 1932, "A different way of performing iridectomy in glaucoma," in 1935, and "Un caso de reabsorption espontanea de la catarata con glaucoma secondaria," in 1939. De Ocampo with Cruz published "Dark adaptation in adult beriberi," in 1940, and de Ocampo, "Epithelial dystrophy due to hypovitaminosis," in 1941.

Japanese occupation

The gains in Philippine ophthalmology acquired during the American regime suffered a severe setback during the blackout of the Japanese occupation. Not only was there a shortage of most ophthalmologic necessities, including the ophthalmic instruments and equipment in the Philippine General Hospital and San Juan de Dios Hospital, but even equipment and instruments of private practitioners of ophthalmology were either lost or destroyed. The contributions to ophthalmologic literature by Filipinos were at a standstill. There was even an epidemic of retrobulbar neuritis among Filipinos. "A case of phlebitis and periphlebitis retinae" was reported in The American Journal of Ophthalmology by de Ocampo in March, 1942. Some Japanese ophthalmologists with the Japanese Imperial Army occasionally visited the Philippine General and other hospitals.

Liberation and preindependence era

The short period from February, 1945, to July, 1946, saw a revival in the practice and teaching of Philippine ophthalmology but still it was combined with otolaryngology. Only Dr. Lucio Abad, who was trained in Japan, practised otolaryngology only. The American ophthalmologists with the Armed Forces of Liberation were instrumental not only in replenishing by donation or otherwise the instruments and equipment in the medical schools but they also stimulated scientific meetings. They helped by encouraging us and by placing some of our men in refresher and trainee courses in American ophthalmologic centers. Among those who should be mentioned are Dr. Brittain F. Payne of the New York Eye and Ear Infirmary who was consultant ophthalmologist to the U. S. Air Forces, and Dr. Tinkess of Columbia-Presbyterian of New York.

It was during this period, on November 25, 1945, that the Philippine Ophthalmological and Otolaryngological Society was formed through the initiative and efforts of A. S. Fernando who became its first president. The other officers were: vice president, E. Reyes; secretary-treasurer, J. N. Cruz; directors, G. de Ocampo, G. Farrales, J. Eusebio, and T. Ilano.

Independence era

The impetus given to Philippine ophthalmology during the liberation was continued in the early Independence Era (July 4, 1946, to now). Many of our eye, ear, nose and throat men went to the United States on fellowships in ophthalmology, or on their own.

The problems of Philippine ophthalmology were presented in a paper, "Ophthalmological problems in the Philippines"[5] by de Ocampo before the staff of the Institute of Ophthalmology, Columbia-Presbyterian Medical Center on April 12, 1947. Among the things he mentioned were: "Our foremost ophthalmologic problem in my opinion, is the training of men. We need more fellowships in ophthalmology. We need buildings in which to work and tools to work with. We need libraries in ophthalmology. . . . We do not as yet have a separate Department of Ophthalmology in the two colleges of medicine in the Philippines, and I believe that we need men who should devote their full time to ophthalmology. . . . One of our most important tasks is to learn your technique, your procedures, your practices, your setup and the use of your tools, many of which we at present lack. We have to develop Philippine ophthalmology along

American patterns with your help. Lastly we need consultants."

Nicolas-Fernando[10] said in 1953: "From 1947 when those who had gone to the United States for specialized training began to arrive, there has been a tendency to separate the specialties. For example, since his arrival in 1947, de Ocampo has limited his practice to ophthalmology (the first physician to do this since Alberto, in 1905, returned from Europe to practice ophthalmology but began to practice eye, ear, nose and throat in 1914). In 1952, de Ocampo established the first ophthalmic hospital in the Philippines. Despite this tendency, however, the number of those who practice the combined specialties is still much greater than those who devote themselves exclusively to either ophthalmology or otolaryngology."

As a matter of fact, in "What we may learn from the American ophthalmologists,"[9] de Ocampo stated before the Philippine Ophthalmological and Otolaryngological Society on September 27, 1947, "Now that the Philippines is an independent nation, it seems worth our while to catch up with American standards and leadership; and I firmly believe that some of us must concentrate on ophthalmology alone if we hope to raise the standards of practice, teaching, and research in Philippine ophthalmology."

Perhaps to follow this advise, many of our young physicians who have gone abroad have taken up only ophthalmology and have come back. Among the first of them may be mentioned H. Velarde, Jr. in 1950, S. Lopez in 1951, and E. Caparas in 1953. Others followed—Mangubat and Lim in 1955, Batungbacal in 1957, A. Fernando, Jr., A. N. Fernando, and E. Almeda in 1958. Others who have taken ophthalmologic training in the United States and Europe are concentrating on ophthalmologic practice and there are still many at present specializing only in ophthalmology in the United States.

Philippine ophthalmologic literature

During the Spanish Colonial Era, no article on ophthalmology can be found. Even Rizal wrote only one scientific medical article,[1] which is not on ophthalmology. I have mentioned the important ophthalmic articles contributed by the early American ophthalmologists and those of the Philippine eye, ear, nose and throat physicians during the American and Japanese occupations. It is worthy of note that Ubaldo published two articles in The American Journal of Ophthalmology on the "Biography of Rizal" and the "Intracapsular extraction of cataract after the Barraquer technique," in 1923 and 1924. Fernando had an article in the *Archives of Ophthalmology* on the "Causes of blindness among Filipinos" and "Survey of clinical cases in the P.G.H. dispensary," in 1922 and 1923. All the others were published in the *Journal of the Philippine Medical Association, San Juan de Dios Bulletin, Colegio Medico-Farmaceutico Bulletin,* or *Actas y Memo Asamblea Regs.*

During the Independence Era, more Filipino contributions to our ophthalmologic literature appeared. Those who contributed articles in journals abroad were de Ocampo, et al., on "Epidemic retrobulbar neuritis in the Philippines during the Japanese occupation," in The American Journal of Ophthalmology in June, 1947; "Latent nystagmus following head injury," in the *Archives of Ophthalmology* in June, 1947, and "Di-isopropyl fluorophosphate (DFP) in cycloplegic refraction," in The American Journal of Ophthalmology in 1951; Nañagas on "Corneal lesions due to hypovitaminosis" in the *Archives of Ophthalmology;* Vicencio on "Polyethylene tube in lacrimal sac infection," and "Sclerocleisis" in The American Journal of Ophthalmology and *Archives of Ophthalmology.* Sayoc has recently published several articles on the "Surgery of ptosis," "Slit palpebral aperture," and "Blepharochalasis" in The American Journal of Ophthalmology; Lopez, "Use of cortone in external ocular diseases" in the *Archives of Ophthalmology,* and Batungbacal on "Cycodiathermy," in The American Journal of Ophthalmology.

The Philippine Ophthalmological and Otolaryngological Bulletin published its first number on September 14, 1946, with A. S. Fernando as its first editor. It became a "Real medium of our scientific activities and productions."[10] Then it was changed to *Philippine Journal of Ophthalmology and Otolaryngology* in January, 1955. Most of the papers read at the Philippine Ophthalmological and Otolaryngological Society bimonthly and annual meetings were published here.

Although the majority of the papers were on clinical ophthalmology and consisted of case reports and experiences with standard clinical procedures or operations, they showed a somewhat different nature from those contributed to such other local journals as the *Acta Medica Philipina,* the *P.M.A. Journal,* the *Journal of the Philippine College of Surgeons,* the *Bulletin of the College of Medicine of the University of St. Tomas,* the *Journal of the Philippine Federation of Private Medical Practitioners,* and the *M.D. Journal.* Many of the articles in the latter journals were written for the general medical practitioners but quite a number were directed to local ophthalmologists and eye, ear, nose and throat medical practitioners.

By this time several articles appeared which are real contributions to clinical ophthalmology in this country. Among these may be mentioned those of de Ocampo, "A re-examination of the trachoma-follicular conjunctivitis problem in the Philippines," which won the Manila Medical Society Award on Clinical Research in 1954; and his other articles on cataract surgery, glaucoma, pterygium, corticoids and corneal transplantation; Tamesis on corneal transplantation and the use of polyethylene tubes in glaucoma, and some investigations on the central regulating mechanisms of glaucoma; Quilala on beta irradiation and pterygium; Lim on epithelial invasion of the anterior chamber; Legasto on radiation of retinoblastoma.

Several of these articles have been abstracted in foreign journals of general or ophthalmologic nature, while others are cited in recent textbooks in ophthalmology. But it is quite evident that a great amount of our ophthalmologic literature is for general medical practitioners. The majority of contributions are case reports, local experiences, statistics, or analyses of known clinical procedures or operations. Very meager indeed are real investigations or research on problems of clinical ophthalmology. Very meager or nonexistent are papers on basic ophthalmology.

Some recent contributions from the Philippines to clinical ophthalmology, on corneal transplantation, vascularization, new methods of suturing, new corneal dissector for lamellar keratoplasty, and new operations of posterior lamellar keratectomy, were read by de Ocampo at the XVIII International Congress at Brussels. A. Fernando, Jr., has done some research on the use of radioisotopes in the study of uveitis which has not yet been published.

Ophthalmologic institutions

During the latter part of the Spanish Era, ophthalmology was a separate department and clinical subject in San Juan de Dios Hospital and College of Medicine of the St. Tomas University. During the American regime, ophthalmology in the Philippines began to be tied up to otolaryngology. After liberation from the Japanese and at the beginning of the Independence Era, there were signs of rebirth or liberation of Philippine ophthalmology from the eye, ear, nose, and throat. Although there are now separate Sections of Ophthalmology in the University of the Philippines and University of the East, in the University of St. Tomas and Far Eastern University there is no such division. The Manila Central University holds the distinction of having the first Department of Ophthalmology in the Philippines.

The first Eye Clinic in this country was set up after the liberation, in August, 1947,

at St. Cruz Building and the first Eye Hospital in the Philippines was established in 1952 by de Ocampo at Isaac Peral. The Philippine Eye-Bank was formed by de Ocampo, Tamesis, and Higgins in 1951. It sponsored the first Sight-Saving Week celebration in 1953. The first corneal transplantation in the Philippines was done on August 3, 1949, "A milestone in ophthalmic surgery in the Philippines," according to Nicolas-Fernando.[1]

The first Specialty Board in the Philippines that of the Philippine Board of Ophthalmology and Otolaryngology was formed in January, 1954, with G. de Ocampo as chairman, J. Tamesis as secretary and E. Reyes, J. N. Cruz, T. F. Garcia, and M. G. Tan as members. De Ocampo, Tamesis and Reyes formed the Section on Ophthalmology, while Tan, Garcia, and Cruz that on otolaryngology.

An Eye Institute is still a dream in this country but separate eye departments in all of our colleges of medicine are bound to come. It is just a matter of time.

Philippine ophthalmologic diseases

In 1955, de Ocampo read a paper at the Philippine Ophthalmological and Otolaryngological Society annual meeting on "Some observations on geographic and racial ophthalmology in the Philippines."[6] He discussed the eye diseases in the Philippines, reported their incidence, peculiarities and characteristics. He called attention of Philippine ophthalmologists to further investigation in this field.

National and international ophthalmology

Until recently Filipino ophthalmologists have been directing their attention only to the national aspects of ophthalmology. In the precolonial and colonial eras individual ophthalmologists worked on their own or were connected with teaching institutions. In 1945, the Philippine Ophthalmological and Otolaryngological Society combined the elements of different institutions into a common group. Filipino ophthalmologists or eye, ear, nose and throat practitioners attended the XVII International Congress of Ophthalmology in New York in 1954 but none presented a paper. At the XVIII International Congress of Ophthalmology in Brussels in September, 1958, for the first time at such international congresses of ophthalmology, a Philippine ophthalmologist presented a paper and showed surgical films on keratoplasty. These surgical films were given first award at the congress of the Philippine College of Surgeons on December 6, 1958, in the first competition on locally produced surgical movies. Philippine ophthalmic surgery seems not to be behind but rather in the lead in this respect among other surgical specialties in the Philippines.

It must be mentioned that Tamesis was invited to read a paper on keratoplasty at the last meeting of the International College of Surgeons in 1957 in the United States. Then, also, at the XVIII International Congress of Ophthalmology in Brussels when the Asia-Pacific Academy of Ophthalmology was organized, we were given its first presidency and Manila was chosen the site of its first congress (1960). After having been put in the world ophthalmologic map the Philippines is now given the opportunity to show what level of ophthalmology there is in this part of the globe.

The Philippine Ophthalmological Society

The Philippine Ophthalmological Society was organized on October 24, 1958. Fourteen Filipino physicians dedicating most of their time to ophthalmology formed its nucleus. The officers elected were president, G. de Ocampo; vice president, J. Tamesis; secretary treasurer, E. Almeda; councilors, E. Caparas and B. Sayoc.

The Philippine Ophthalmological Society is the culmination of an evolution in Philippine medicine which has started since the Philippines became independent. As you will

recall, Philippine ophthalmology like European ophthalmology was free from the bond with otolaryngology until the Americans came. Now, like a rebirth, Philippine ophthalmology has declared its freedom from the EENT tradition.

The ideal of Philippine ophthalmology was stated by de Ocampo in January, 1950, during the fifth inaugural meeting of the Philippine Ophthalmological and Otolaryngological Society,[5] "I hold that the ultimate goal of Philippine ophthalmology should be that any Filipino with an eye disease is given adequate treatment and that no blindness should come to any Filipino without the benefit of modern ophthalmologic knowledge and practice."

This ideal is embodied in the aims of the Philippine Ophthalmological Society. Our ultimate objective is service to eye patients. While it encourages limitation of practice it does not require complete limitation, nor has it any taint of exclusiveness based on the fortunes of training or the glamor of titles. Ours is an ophthalmological society where service and dedication to ophthalmology are above that of the limitation of the practice of ophthalmologists. I believe that limitation of practice to ophthalmology is a means to an end and not an end in itself. Our primary concern is the subject of ophthalmology, knowing that the practice and science of ophthalmology and particularly Philippine ophthalmology will continue after the present generations of Philippine ophthalmologists have passed away.

The separation of ophthalmology from otolaryngology is likewise not an end in itself but a means to an end, that of more dedication to and concentration on ophthalmology and its cultivation so that it will be better able to relieve blindness. Hence the more complete the disentanglement of the Philippine Ophthalmological Society from association with otolaryngology, the more free it will be to chart its own course toward its destiny.

The Philippine Ophthalmological Society has become a member of the Asia-Pacific Academy of Ophthalmology and is now preparing to be host to the first congress to be held in Manila in 1960.

Conceived a decade ago and born on United Nations day, October 24th, the Philippine Ophthalmological Society ushers an era of international ophthalmology into this country. It is being christened or inaugurated today with the blessings of the dean of contemporary Philippine medicine, Dr. A. G. Sison, who has in many ways done much for Philippine ophthalmology. I recall that in 1941, Dr. Sison offered me a fellowship to give up ophthalmology for neurology and psychiatry. After accepting it, I rejected it the next day and he was understanding enough to say that the gain to Philippine ophthalmology means a loss to Philippine neurology. I waited for another chance. When five years later, in 1946, I received the Kellogg Fellowship for ophthalmology and bronchoesophagology, he looked for another man to take up bronchoesophagology. That was when I gave up eye, ear, nose, and throat for ophthalmology.

I shall end this historical survey by quoting from the Bible, "The first shall be last and the last shall be first." If ophthalmology is the oldest specialty in medicine and the last to be organized in this country, it aims to be first in the future.

932 Isaac Peral.

References

1. Bantug, J. P.: A Short History of Medicine in the Philippines: During the Spanish Regime 1565-1898. Manila, Colegio Medico-Farmaceutico de Filipinas, Inc., 1953.
2. Bettmann, O. L.: A Pictorial History of Medicine. Springfield, Ill., Thomas, 1956.
3. de la Gironiere, P. P.: Twenty Years in the Philippines. (Translated from the French.) New York, Harper and Brothers, 1954.
4. de Ocampo, G.: Ophthalmological problems in the Philippines. J.P.M.A., **23**:619-621 (Dec.) 1947.

5. ———: Ideals and problems of Philippine ophthalmology. J.P.M.A., **26**:355-362 (Aug.) 1950.
6. ———: Some observations on geographic and racial ophthalmology in the Philippines. Philip. J. Ophth., **7**:6-11 (Jan.-Mar.) 1956.
7. ———: Dr. Rizal, Ophthalmic surgeon. U.P. Medic's Newsette, **3**:2-6 (Dec.) 1954.
8. ———: Rizaliana on cataract. Philip J. Surg., Obstet. & Gynec., **13**:125-134 (Mar.-Apr.) 1958.
9. ———: What we may learn from the American ophthalmologists, J.P.M.A., **24**:15-18 (Jan.) 1948.
10. Fernando, F. N.: Ophthalmology and otolaryngology in the Philippines from 1903-1953. Golden Book Philip. M. A., Manila, 1903.
11. Lopez-Rizal, L.: Personal communications.
12. Onsendoort, A. G.: Historia de la ophthalmologia (Compendia hasta 1838. Traduccion del Aleman). Laboratories del Norte de España, S.A., Barcelona, 1947.
13. Rizaliana Exhibit, June 19-30, 1958, held in connection with the Golden Jubilee Celebration, University of the Philippines, 1908-1958, No. 151-160, p. 12.

CHYMOTRYPSIN IN VARIOUS OPHTHALMIC SURGICAL PROCEDURES

WENDELL L. HUGHES, M.D., EARL L. LEWIS, M.D., AND JOSEPH AMDUR, M.D.
Hempstead, New York

Medical therapy is progressing from the use of broad spectrum medications to drugs with a specific effect on one end-organ.[1] With this change to specific drugs, have come the concept and usage of enzyme therapy. Clinically, one of the most useful group of enzymes has been the proteolytic, and of these trypsin and chymotrypsin are best known.

A concept of proteolytic enzyme therapy has evolved from a number of investigations.[2-5] It is based upon the premise that the absorption of an inflammatory exudate is delayed by the blockage of capillaries and lymphatics with large protein complexes. These macromolecular proteins are found in and around any area of injury, occurring as an integral part of the normal inflammatory response. Because of their large size, these proteins act to dam the lymphatics and capillaries, thereby delaying absorption of edema and inflammatory debris.

The enzymes trypsin and chymotrypsin digest complex proteins into smaller, easily absorbed carbon fragments. Lymphatics and capillaries are cleared of these proteins and fluid is withdrawn from the area of inflammation. Thus the enzymes reduce the inflammatory response and are a secondary aid to the concentration of other specific medications, such as antibiotics at the site of injury. Viable proteins are not attacked when the enzymes are delivered to the wound in therapeutic concentrations.[6]

This concept has been amply tested in general medicine and surgery. The proteolytic enzymes have reduced inflammation in athletic injuries,[7] hematomas[8] and burns, thrombophlebitis,[9] asthma[10] and many types of surgical wounds. Many more applications for their use are being studied.

In ophthalmology, the use of chymotrypsin has been reported in uveitis, hyphema, vitreous hemorrhage and retinal hemorrhage.[11] In orbital trauma, swelling and ecchymosis are rapidly reduced with systemic chymotrypsin. Proteolytic therapy of obstruction of the nasolacrimal duct and corneal ulcers is presently being evaluated. Enzymatic zonulolysis in cataract extraction is receiving much attention.

PRESENT STUDY

The present study was undertaken to evaluate systemic chymotrypsin as a routine proteolytic, anti-inflammatory agent in a variety of ocular surgical procedures.

MATERIAL AND METHOD

One hundred fifteen cases were operated upon consecutively by one of us (W. L. H.). These included 41 muscles, 28 plastic ophthalmic procedures, 39 lens (six combined

TABLE 1

RESPONSE TO INTRAMUSCULAR CHYMOTRYPSIN

Procedure	No. Cases	More Reaction	Average Reaction	Less Reaction	% Cases with Less Reaction
Muscles	41	2	12	27	66.0
Plastics	28	0	14	14	50.0
Lens	39	2	24	13	33.3
Corneal	7	0	7	0	0.0
Total	115	4	57	54	47

with iris inclusion-anterior sclerectomy) procedures and seven corneal transplants. No surgical case was excluded from the study. Controls consisted of the amount of reaction normally expected to occur by the same surgeon using the same general technique over the past 30 years. One cc. of aqueous chymotrypsin* was administered intramuscularly at the conclusion of the surgical procedure, and a second cc. was given intramuscularly the following day with a 21-gauge needle. The patients reported that there was little immediate or delayed pain at the injection site.

The operated eye was carefully observed and the amount of edema and tissue reaction was recorded by the surgeon. The responses were divided into (1) average reaction, (2) more than average reaction, and (3) less than average reaction.

Average reaction meant that the tissue reaction was insignificantly altered by the injections of chymotrypsin or the reaction was about the same as normally expected.

More reaction meant a greater than normal amount of tissue reaction incurred by the same surgeon using the same technique, even in the presence of systemic chymotrypsin.

Less reaction meant that, on the basis of previous experience of the same surgeon using the same technique, there was a very distinct and well-defined diminution in the amount and duration of tissue reaction (the only variable having been introduced being systemic aqueous chymotrypsin). If this decrease was not clearly evident, the case was recorded as having average reaction.

The results are summarized in Table 1.

DISCUSSION

An evaluation of the results discloses that 66 percent of the muscle cases had less than average amount of expected reaction. This figure confirms the over-all clinical impression of the study.

The greatest anti-inflammatory effect of the drug was readily apparent in cases where more than two muscles were operated upon, especially following surgery on the inferior oblique where there is usually considerable reaction. One case, that of a 29-year-old man with a history of previous horizontal muscle surgery in the same eye, required surgery on five muscles at recent operation. Because of the previous surgery and the extensive surgery at this subsequent procedure, a marked reaction was expected postoperatively. With the usual dose of systemic chymotrypsin, he had no more reaction than that ordinarily following a recession-resection operation. This case was therefore recorded as one with less than average reaction.

In myectomy of the inferior oblique, our usual technique is to excise completely a portion of the muscle after the sheath has been opened. There is usually moderate hemorrhage from the cut ends of the muscle. Since dissection is carried down to and beyond the inferior orbital rim, there is an extensive plane into which the hemorrhage seeps, frequently causing considerable postoperative

* Supplied as Chymar Aqueous by the Armour Pharmaceutical Company, courtesy of Dr. J. A. Hubata, medical director.

ecchymosis and edema of the lower lid. After instituting systemic chymotrypsin into the surgical routine, the amount and duration of the postoperative ecchymosis and edema were materially lessened.

In plastic procedures, 50 percent of the cases had less than the usual amount of postoperative reaction. However, it is our practice to place a wrap-around pressure headdressing on all plastic cases with the first dressing done on the fifth to seventh postoperative day. At that time, normally, the amount of reaction is minimal even in untreated cases.

In cataract extractions (and in the combination cataract extraction with iris inclusion and anterior sclerectomy), 33.3 percent of our cases were rated as having less than average reaction with systemic chymotrypsin. We feel this figure may be misleadingly low. The amount of lessened reaction is difficult to appraise in the usual cataract extraction where some lid edema and ciliary injection are often the only reactions present in patients not treated with chymotrypsin. The lessened reaction in the treated cases as compared with untreated cases appeared to be of definite clinical significance. The statistics showing that one-third of the cases were improved with the enzyme were considered to be conservative. It is worthy of note that in this treated series only two patients had any more than an average reaction, since in any routine series a larger number of cases would normally be expected to have more than average reaction.

Reactions

There were no untoward systemic reactions from the intramuscular chymotrypsin. No patient experienced pain, hyperpyrexia, chills, erythema or dermatosis. However, while this study was in process, we had the opportunity to treat a 50-year-old woman with posterior uveitis—etiology unknown. Part of her therapy consisted of buccal tablets (chymotrypsin). On the second day of this therapy, she developed urticaria, wheals, and erythema progressing to an exfoliative type of dermatitis affecting particularly the hands, feet and buccal mucous membrane. This cleared slowly on withdrawal of the buccal chymotrypsin and steroid therapy over a period of four or five weeks.

Although no patient in our series of 115 cases given intramuscular chymotrypsin developed an untoward reaction, Liebowitz and Ritter[12] recently reported an almost fatal anaphylactic reaction to aqueous chymotrypsin. They treated a 44-year-old man for epididymitis with 17 intramuscular injections of this drug. Within five minutes after the last injection, he developed a classical acute anaphylactic syndrome, progressing to pulmonary edema, coma and shock. Fortunately, the patient responded to the prompt heroic therapy which was instituted. Our purpose in including these two cases in this report is to warn others of the rare but possible occurrence of an anaphylactic reaction.

Summary

A total of 115 consecutive ophthalmic surgical cases were treated with the anti-inflammatory or proteolytic enzyme, chymotrypsin. This was administered in an aqueous suspension intramuscularly on the day of operation and on the first postoperative day. In 66 percent of the muscle cases, 50 percent of the plastic cases and 33.3 percent of the lens cases there was a less than average postoperative inflammatory reaction with this therapy. No untoward reactions occurred in the series. The greatest anti-inflammatory effect of this drug was manifested in multiple muscle surgery and was particularly noticeable in surgery of the inferior oblique where there had been considerable swelling in the untreated cases. It was also quite noticeable in intraocular surgery.

Conclusion

It is felt that the results are encouraging and this therapy would be particularly advantageous in cases in which normally one would expect considerable postoperative re-

action. Further investigation to gather a larger series is of course in order and the investigation is continuing. It is hoped that others will be stimulated to try this therapy and report their results in the future. At present we are evaluating the oral chymotrypsin (Chymoral) and the buccal preparation in various ophthalmic surgical procedures.

131 Fulton Avenue.

We wish to thank the Armour Pharmaceutical Company, the nurses, and the preceptor on the Eye Service of the Hempstead General Hospital for their valued co-operation in this study.

References

1. Rymenant, M. V., et al.: Enzymes in clinical medicine. New England J. Med., **261**:1325 (Dec.) 1959.
2. Menkin, V.: Dynamics of Inflammation. New York, Macmillan, 1950.
3. Day, T. D.: The localizing action of fibrinous exudates. Brit. J. Exper. Path., **35**:315-321, 1954.
4. Martin, G. J.: Anti-inflammatory effect of trypsin: Ann. N.Y. Acad. Sci., **68**:70-88, 1957.
5. Innerfield, I.: The anti-inflammatory effect of parenterally administered proteases. Ann. N.Y. Acad. Sci., **68**:167-175, 1957.
6. Connell, J. E., and Rousselat, L. M.: The use of enzymatic agents in the debridement of burn and wound sloughs. Surgery, **30**:43, 1951.
7. O'Donoghue, D. H.: General principles involved in the treatment of injuries in athletes. M. Times, **87**:1246-1260 (Oct.) 1959.
8. Morani, A. D., Serlin, O., King, R., and Flynn, J.: Clinical experiences with enzyme (Chymar) therapy in wound healing. Proc. Internat. Cong. Plastic Surg., London, July 12-17, 1959.
9. Davis, O. F., Levine, A. J., Beck, C., and Horowitz, B.: Clinical pharmacological evaluation as an anti-inflammatory enzyme. Postgrad. Med., **26**:719-723 (Nov.) 1959.
10. Parsons, D. J.: Asthma, bronchitis, rhinitis and sinusitis: Adjunctive treatment with intramuscular chymotrypsin. Clin. Med., **5**:1491 (Nov.) 1958.
11. Jenkins, B. J.: J.M.A. Georgia, **45**:431 (Oct.) 1956.
12. Liebowitz, D., and Ritter, H.: Anaphylactic reaction to chymotrypsin. J.A.M.A., **172**:159, Jan. 9, 1960.

USE OF INTRAMUSCULAR CHYMOTRYPSIN IN CONTROLLING TISSUE REACTION FOLLOWING STRABISMUS SURGERY

A PRELIMINARY STUDY

EDWARD G. FORTIER, M.D.
Lombard, Illinois

Every so often the pharmaceutical laboratories will introduce a new product which offers unique advantages to the ophthalmologist. A recently introduced proteolytic enzyme, chymotrypsin,* appears to be such a product.

It is claimed that (a) chymotrypsin will minimize traumatic edema of most any type; and (b) toxicity, allergy, contraindications or other objections are for the most part nonexistent with this drug. Certain precautions to be observed, such as nonuse in liver disease, deep intramuscular injection, and so forth, are no more serious or numerous than with many other drugs already in general use.

One form of traumatic edema that is especially important to the ophthalmic surgeon is the postoperative reaction. Because of the confined space in which he works, postoperative edema contributes to his patient's disability and discomfort in practically every instance; on occasion, edema as such may be a factor in an operative failure. The availability of chymotrypsin, which offers the possibility of minimizing operative reaction in an apparently safe manner, seemed to require some investigation of its effect following ocular surgery.

* Chymar®, and Chymar Aqueous®, The Armour Pharmaceutical Company, Kankakee, Illinois. Both represent 5,000 units of proteolytic activity per cc.

It is the purpose of this paper to present some introductory clinical studies in which chymotrypsin was utilized following major extraocular surgery, together with the presently available clinical and experimental evidence upon which this chemical's action is based. Results of the clinical studies in this series are recorded objectively by postoperative photographs taken during the convalescent period in order that any significant findings may be conveyed to other ophthalmic surgeons.

Available literature

The efficacy of chymotrypsin in reducing inflammation from most any cause is based on experimental data obtained after the production of a variety of traumatic inflammations in mice, rats, and guinea pigs. The resulting edema was compared and evaluated by the use of treated and control animal groups in each instance by weighing affected extremities, or by comparing skin erythema. A few examples of these animal data follow:

1. Turpentine, 30 percent in peanut oil, was injected under the plantar aponeurosis of the forelegs in mice. One group of mice was treated with various amounts of chymotrypsin, and the other group served as controls; weights of the forelegs after amputation on the third day served as the determining factor. The most significant effects were seen in mice receiving 1,000 units of chymotrypsin.

	Weights	
Mouse No.	*Controls* (mg.)	*Chymotrypsin* (mg.)
1	490	320
2	620	330
3	630	460
4	580	390
5	640	370
6	560	480
7	610	490
Average weights	590	405

2. A similar inflammation was produced in the forelegs of guinea pigs by injecting 50-percent turpentine in peanut oil; after the inflammation had become manifested, 4,000 units of chymotrypsin were injected into each pig.

Results	*Guinea Pig Control* (gm.)	*Guinea Pig Treated* (gm.)
1	13.32	9.80
2	11.67	8.76
3	11.75	10.12
Average	12.25	9.56

This experiment tends to illustrate the efficacy of chymotrypsin even when it is utilized after the inflammation has become manifested.

3. A similar inflammation was produced in the forelegs of rats, using 50-percent turpentine in peanut oil; 4,000 units of chymotrypsin was then administered in six divided dosages.

Rat No.	*Control* (mg.)	*Treated* (mg.)
1	5890	5010
2	5980	5120
3	5790	5220
4	6000	5230
Average	5915	5145

This experiment tends to show that continuous, divided dosages of chymotrypsin spread over a fairly long period enhances the possible effects to be gained by this enzyme.

In the human, it has been shown that chymotrypsin has a greater anti-inflammatory action than trypsin,[1] and that chymotrypsin is less toxic by rapid administration than is trypsin.[2]

Chymotrypsin has been used successfully as a mucolytic agent to reduce peribronchial and intrabronchial edema.[3] Another investigator[4] reports that chymotrypsin acts as an anti-inflammatory agent and hastens the absorption of edema and of blood in the tissues. In a recently published study[5] chymotrypsin is reported to have produced good to marked improvement in 48 of 60 chronic cases of asthma, bronchitis, rhinitis and sinusitis. Used together with appropriate antibiotics,[6] this enzyme has given good results in the treatment of chronic otitis, chronic mas-

toid, chronic maxillary sinus, chronic frontal sinus, chronic ethmoid sinusitis, eustachian tube synechia, otitis adhesions, diphtheria membrane, croup, and laryngitis edema.

Present clinical studies

Evaluation of an enzyme such as chymotrypsin in ophthalmic surgery presents several problems. There is no way to obtain adequate control material since the fellow eye would constitute the best available control. It, of course, is equally affected by this systemically injected enzyme.

Further, individual variations are present in tissue reactions to surgery, as well as some variation in degree of trauma from case to case. These objections can be minimized by studying and comparing cases of similar operations done by a single surgeon, as is done here.

Also, the size of the orbit varies from age to age, although the trauma remains relatively constant; I have observed in my own cases that small children experience much more apparent reaction than do older patients. Therefore, the final evaluation of chymotrypsin will depend upon many clinical observations, and this paper is meant to be only an introduction.

I first used this preparation following minor procedures such as chalazion excision. After observing what appeared to be objective lessening of lid edema on three successive occasions, I decided to try chymotrypsin after a major extraocular procedure. Since I routinely obtain pre- and postoperative photographs on my strabismus cases, circumstances were ideal for recording the possible effects of chymotrypsin following eye muscle surgery.

Cases chosen were limited to those subjected to maximum surgical trauma; medial rectus recession together with lateral rectus resection was the minimum included in this study; in most instances one or both inferior oblique muscles were also recessed, and in most of the cases here reported both eyes were operated upon. At this time, I have five such qualifying cases, and three control cases for illustration. As noted in the legends, the photographs were taken at varying intervals postoperatively because in starting out I had no idea which interval would be the most informative. Four and 15 days postoperatively appear to be the intervals at which the effects of chymotrypsin can be best demonstrated.

Methods and Dosage

The dosages of chymotrypsin used were two cc. intramuscularly on the operating table or shortly after the patient was returned to the recovery room. On the first postoperative day, one cc. of chymotrypsin was given in the morning, and repeated in the afternoon. The patient was seen in the office on the third or fourth postoperative day when two cc. of chymotrypsin were again administered. On the sixth or seventh postoperative day another two cc. of chymotrypsin were administered to some of the cases in the treated group. A slight variation in the day of administration of chymotrypsin after the patient was discharged from the hospital was necessary because on occasion the originally intended day fell on a Sunday, and it was not possible to see these patients on that day. Also, the last three patients in the treated group received only three injections of chymotrypsin because the experimental animal data indicated that the greatest value from this chemical tended to be accomplished in the early postirritant phase. It is interesting to note that comparison of the studies revealed that this appears to be correct, and the injection of chymotrypsin in the last four to seven days of postoperative convalescence does not apparently change the degree of reaction to any extent.

Clinical results

Treated cases

Five cases are presented which were treated with chymotrypsin following strabismus surgery.

CASE 1

Fig. 1-A (Fortier) Pre-op. status: Marked esotropia + vertical imbalance in 17 yr. old male.

Fig. 1-B (Fortier) Sixth post-op. day after surgery on both medial recti, both lateral recti, and left inf. oblique muscles.

Fig. 1-C (Fortier) Fourteenth post-op. day: Almost complete recovery except for minor conjunctival injection.

CASE 2

Fig. 2-A (Fortier) Pre-op. status: Exotropia present from childhood in a 32 year old female.

Fig. 2-B (Fortier) Seventh post-op. day after surgery on both medial recti and both lateral recti. Eyes open and comfortable.

Fig. 2-C (Fortier) Fifteenth post-op. day: Swelling of lids and conjunctiva almost entirely abated.

CASE 3

Fig. 3-A (Fortier) Pre-op. status: Marked esotropia and left vertical imbalance in an 8 yr. old male; left eye is partially amblyopic.

Fig. 3-B (Fortier) Fourth post-op. day after surgery on both medial recti, both lateral recti, and left inf. oblique muscles.

Fig. 3-C (Fortier) Fourteenth post-op. day: Moderate ecchymosis persists but lid edema is well controlled by Chymar.

CASE 4

Fig. 4-A (Fortier) Pre-op. status: 20 degree esotropia and moderate vertical imbalance in an 8 yr. old male; deformity has persisted despite intensive orthoptic management elsewhere. Left eye is completely amblyopic with vision correctable to only 20/300.

Fig. 4-B (Fortier) Fourth post-op. day after surgery on both medial recti, both lateral recti, and left inf. oblique muscles.

Fig. 4-C (Fortier) Twelve days post-op: Chymar was only given on day of surgery in this case; lid edema is subsiding faster than on controls but better results were secured when Chymar is used for 48-56 hours after operation.

CASE 5

Fig. 5-A (Fortier) Pre-op status: Marked esotropia + slight vertical imbalance in 13 yr. old girl who had been unsuccessfully operated elsewhere at 5 yrs. of age.

Fig. 5-B (Fortier) Eight days post-op. after surgery on both medial recti, both lateral recti, and right inferior oblique muscles.

Fig. 5-C (Fortier) Sixteen days post-op; only slight subconjunctival ecchymosis and minimal lid edema remaining.

CONTROL A

Fig. A-1 (Fortier) Pre-op status: Bilateral esotropia + left vertical imbalance in six yr. old male; left eye is amblyopic.

Fig. A-2 (Fortier) Seventh post-op. day after surgery on left medial rectus, left lateral rectus, and left inf. oblique muscles.

Fig. A-3 (Fortier) Sixteenth post-op. day: Without Chymar, recovery is still far from complete.

CONTROL B

Fig. B-1 (Fortier) Pre-op status: Infantile comitant esotropia in 11 month old infant.

Fig. B-2 (Fortier) 3 months post-op: Without Chymar, lids were swollen closed for over 2 months; complete recovery required 4 months.

CONTROL C

Fig. C-1 (Fortier) Pre-op status: Comitant exotropia + vertical imbalance in 18 yr. old male present since early childhood. Right eye is completely amblyopic.

Fig. C-2 (Fortier) 2 months post-op: Without Chymar, lids of right eye remain swollen following surgery on right medial and lateral recti, and right inf. oblique muscles.

CASE 1

Figure 1-A shows a 17-year-old youth with amblyopia and esotropia of the left eye and marked overaction of the left inferior oblique. Bilateral surgery was performed and the postoperative status at six days (fig. 1-B) and 14 days (fig. 1-C) is presented.

CASE 2

Preoperative status of the second treated case is shown in Figure 2-A; a marked exotropia present from childhood was found. Bilateral surgery was performed and Figures 2-B and 2-C illustrate the patient's recovery at the seventh and 15th postoperative days.

CASES 3, 4, AND 5

Figures 3-A, 4-A, and 5-A show preoperation findings approximately similar to those in Case 1. The postoperative progress at the end of the first and second weeks is also shown.

CONTROL CASES

Pictures in the control group illustrate the usual postoperative progress of patients following strabismus surgery. Three cases are presented, in none of which was any chymotrypsin used. It was necessary to take these photographs at longer periods after operation in order to present a comparable degree of recovery from postoperative edema; it is interesting to note, however, that postoperative conjunctival injection was not apparently modified or shortened in duration by treatment with chymotrypsin.

CONTROL CASE A

Figure A-1 presents a six-year-old child with 15 degrees of esotropia. Figure A-2 illustrates recovery at the seventh postoperative day, and Figure A-3, the 14th postoperative day. For the first week this child was not able to open his operated eye and by the end of the second week he could barely do so.

CONRTOL CASE B

Figure B-1 shows an 11-month-old infant with marked esotropia and bilateral vertical imbalances. Figure B-2 records the status 12 weeks postoperative, at which time removery is still not complete.

CONTROL CASE C

Figure C-1 shows an 18-year-old youth with exotropia and marked overaction of the right inferior oblique. Figure C-2 illustrates his protracted recovery at eight weeks postoperative.

DISCUSSION

In discussing chymotrypsin several aspects of this chemical's action should be emphasized so that the full efficiency of the enzyme may be obtained. Although there is no difference in action or dosage, chymotrypsin is now available in two forms. The first form, chymotrypsin in sesame oil, is relatively heat stable and requires no special handling other than to avoid freezing. The newer form of chymotrypsin is an aqueous suspension, and with this the temperature control is most important. Prior to use, the aqueous form of chymotrypsin should be maintained at about 40°C. in a refrigerator, but in no case should it be placed in a freezer or should it be allowed to freeze. In the aqueous form, both extremely low and high temperatures will detract from the chemical's therapeutic efficacy and future investigators could possibly be misled if this aspect is not observed.

The other important aspect of chymotrypsin is the potential pain caused at the site of injection of this substance. In the first cases presented herein, it appeared that pain was a necessary and unavoidable aspect to the use of chymotrypsin. Occasionally, this pain was quite distressing to the patient, especially to little children. Patients on occasion seemed to resent the injection more than the operation. Even at this stage, however, some measure of the efficacy of chymotrypsin can be ascertained by patient reactions. In brief, the treated patients complained of the site of injection of the chemical, but were able to open their eyes and co-operate for adequate ocular examination and inspection. The untreated group, in general, complained of their eyes and were usually unable to co-operate as well in the ocular inspection as a surgeon would prefer during postoperative convalescence.

Concerning the pain at site of injection, the manufacturer claims that, with proper technique, an injection of chymotrypsin can be practically painless. An unusually small bored needle of considerable length was tried and injection by this method was successful. I had been using an 18- or 20-gauge needle

approximately one and three-quarters inches in length; the recommended needle for use in injecting chymotrypsin was 22-gauge, two inches or greater in length. With this needle, it is readily possible to approximate an intramuscular injection and the likelihood of the drug following along the path of the needle as the needle is withdrawn is rendered less likely. With this technique, injection of chymotrypsin has actually proved to be relatively free from distress and quite comparable to injection of such other materials as penicillin suspensions, and so forth.

This technique has made it practical to consider the routine use of chymotrypsin in postoperative ophthalmic surgery. Results presented here also indicate that a further standardization of dosage and/or interval of injection could be pursued with profit.

Conclusions

The results of using chymotrypsin in the postoperative convalescent period following major strabismus surgery can perhaps, more simply, be expressed by the photographic evidence presented. Control cases are supplied for comparison and the individual reader may be able to arrive at a conclusion from the evidence presented. In general, it may be observed that, although postoperative conjunctival injection is not modified nor its duration shortened after treatment with chymotrypsin, postoperative edema is decreased both in amount and duration. However, it should be stated that the photographic evidence cannot express in total the results of a study such as the one presented herein. Even careful photography is not a true substitute for seeing the actual patient.

Most striking from a subjective clinical standpoint was the degree of co-operation and willingness which the treated patients exhibited in permitting early ocular examinations. Completely adequate examinations were accomplished with ease on each of the first four postoperative days. This situation contrasts sharply with the usual reaction. If it can be confirmed by other surgeons, facilitation of early postoperative examinations may be regarded as one of the most important features to be gained through the use of chymotrypsin.

In my opinion, the results presented herein indicate that chymotrypsin exhibits a beneficial effect upon postoperative traumatic response when utilized early in the postoperative period. Further studies are being made. It is hoped that this report will stimulate further investigation by other ophthalmic surgeons. Before the utmost therapeutic efficiency can be effected from a chemical such as chymotrypsin, a definite standardization of interval of injection and dosage used must be established.

Toxicity and Side-Effects

As proteolytic enzymes are protein in nature, occasional reactions are to be expected. These are usually mild, not necessitating discontinuance of treatment. Although sensitivity to chymotrypsin is uncommon, the usual precautions should be exercised in those patients with known allergies or sensitivities.

Summary

1. Use of a systemically administered proteolytic enzyme following strabismus surgery appears to reduce postoperative edema. Preoperative and postoperative photographs of three control cases and five cases treated with chymotrypsin postoperatively are presented as evidence for this observation.

2. Subjectively, patients treated with chymotrypsin appeared to experience much less ocular discomfort in the postoperative period; in addition, they were able to co-operate much better in early postoperative stages and the surgeon's examinations were greatly facilitated.

8 East St. Charles Road.

Acknowledgment

I wish to thank Dr. Joseph A. Hubata, Paul L. Brule, Charles T. Ellis, and James E. Michaels of the Armour Pharmaceutical Company for their help in the preparation of this manuscript.

References

1. Miechowski, W. L., and Ercoli, N.: Studies on proteolytic enzymes: II. Trypsin and chymotrypsin in relation to inflammatory processes. Jour. Pharm. & Exper. Therapeutics, **116**:43, 1956.
2. Hendley, C. D., et al: Studies on proteolytic enzymes: I. Toxicology of crystalline trypsin and chymotrypsin. Arch. Intern. Pharmacodynamie, **106**:164, 1956.
3. Suarez-Diaz, E.: Quimar in the treatment of asthma. Sinopsis Med. Internat., March, 1958, pp. 20-24.
4. Jenkins, B. H.: The use of intramuscular chymotrypsin in ocular conditions. J. M. A. Georgia, October 1956, pp. 431-433.
5. Parsons, D. J.: Asthma, bronchitis, rhinitis and sinusitis; Adjunctive treatment with intramuscular chymotrypsin. Clinical Med., **5**:1491-1494 (Nov.) 1958.
6. Muftic, M. K.: Proteolytic enzymes in otolaryngology. Indian J. M. Sc., **11**:1015-1020 (Dec.) 1957.

AN EXPERIMENTAL INVESTIGATION OF THE BASIC PHENOMENA OF RETINOPEXY*

III. Resistance and capacitive reactance of the cat's cornea, sclera, choroid, and vitreous

Henry A. Knoll,† Ph.D.
Rochester, New York

Introduction

Impedance values for ocular tissues were reported in an earlier paper in this series.[1] It was shown that the impedance of all ocular tissues measured (sclera, choroid, and vitreous) varied inversely with frequency. An attempt was made to construct an electrical analog which would produce the same type of relationship. The data could not be duplicated using fixed-value components in the analog; hence, it was concluded that resistance and the capacitive reactance of these tissues may vary with frequency. That this is true in lysed erythrocytes has been shown by Schwan and Carstensen.[2] The present study was undertaken to test this assumption.

Apparatus

A special head and electrode holder was designed and constructed (fig. 1). The cat's head was held firmly in position by a pair of ear bars and a mouth rod. Two electrode carriers were mounted orthogonally on a semicircular track whose center of curvature could be made to coincide with the center of curvature of either eye of the animal. The electrodes were then always perpendiculuar to the sclera or cornea.

Electrical contact was made in one of two ways: through a pair of electrodes mounted on the electrode carriers, or by using one electrode and a ground return through the ear bars.

Three different types of electrodes were used. They are described in Table 1. Note that the relative areas of the numbered electrodes are indicated by the identifying number. These electrodes were used in various combinations and at separations of 4.0, 8.0 and 12 mm.

The electrical measurements were made using three different techniques:

1. *Bridge method.* A General Radio Twin-T Impedance Bridge, as described by Sinclair[3] was used to balance to null approximately one volt developed across the eye by means of a Hewlett Packard Signal Generator. The signal was applied at frequencies of 0.5, 1.5, 3.0, and 10.0 megacycles.

2. *Phase-angle method.* In this method, the same generator provided either one-half or one volt r.m.s. signal across the eye

* From the Departments of Surgery (Ophthalmology) and Biophysics, University of California Medical Center, Los Angeles 24, California. This investigation was supported by a research grant (B-471) from the National Institute of Neurological Diseases and Blindness, National Institutes of Health, United States Public Health Service, Bethesda, Maryland.

† Present address: Ophthalmic Research and Development Section, Bausch & Lomb Optical Company, Rochester 2, New York.

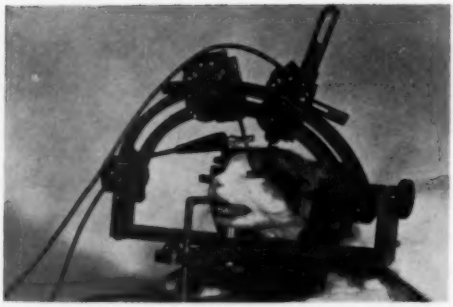


Fig. 1 (Knoll). Cat shown in head holder. Electrodes are applied to the cornea.

at frequencies in the 100 cps to 1.0 mc. range. From the measurements of the voltage developed across the eye, the voltage developed across a resistor placed in series with the eye, and the phase angle between these two voltages measured with a CRT delay sweep circuit, resistance and reactance values were obtained by calculation.

3. *An approximate resistance method.* This method is identical to the phase angle method except that it dispenses with the phase angle measurement. It is essentially the method described in the earlier paper.[1] If a known resistor of large value is placed in series with the eye, approximations to the resistance of the eye may be calculated.

Procedure

Twenty-two adult cats were used as the experimental animals and Nembutal administered intraperitoneally was used as the anesthetic. Except for certain corneal measurements, the temporal portion of the sclera was exposed by means of a large canthotomy. During the course of measurements, the eye was occasionally treated with pontocaine, washed with saline, and turned in its socket to counteract the effects of drying. A single experiment took approximately four hours. The cats were killed after completion of each experiment.

For the first experiment, and those made utilizing the bridge method of measurement, no electrode holder was used. For all other experiments, an electrode holder which provided radial contact of the electrode on the globe of the cat's eye, was used.

Results

Initial experiment

Utilizing the phase angle method of measuring impedance and electrode No. B on the cat's sclera, reactance and resistance values were obtained at frequencies in the 100 cps to 1.0 mc. range. The ear bars served as a ground return; no electrode holder was used. The stiffness of the connecting cable served to hold the electrode against the sclera. A slight, and no doubt variable, pressure was exerted on the eye in this manner. Reasonable visual care was taken to place the electrode in the same position between readings. Approximately one volt rms was applied across the eye, as measured between the electrode and the ear bars. The results are presented in Figure 2.

TABLE 1

Description of electrodes

Number	Description
A	Right-angled, pointed, steel electrode of type used in retinopexy
B	Flat, circular, steel electrode, 2.38 mm. in diameter, of the type used in cyclodiathermy
1	Flat, circular brass electrode, insulated except for a flat end with an area equaling 0.0507 mm.^{2}
3	Flat, circular brass electrode, insulated except for a flat end with an area equaling 0.1521 mm.^{2}
6	Flat, circular brass electrode, insulated except for a flat end with an area equaling 0.3042 mm.^{2}
10	Flat, circular brass electrode, insulated except for a flat end with an area equaling 0.507 mm.^{2}
20	Flat, circular brass electrode, insulated except for a flat end with an area equaling 1.014 mm.^{2}
40	Flat, circular brass electrode, insulated except for a flat end with an area equaling 2.028 mm.^{2}
60	Flat, circular brass electrode, insulated except for a flat end with an area equaling 3.042 mm.^{2}
80	Flat, circular brass electrode, insulated except for a flat end with an area equaling 4.056 mm.^{2}
100	Flat, circular brass electrode, insulated except for a flat end with an area equaling 5.07 mm.^{2}

Straight lines were drawn through the experimental points and they can be given by the following power functions:

$$R = (30.4 \times 10^3)f^{-0.34}$$
$$X = (13.0 \times 10^3)f^{-0.34}$$

Such an equation of the form "$y = a\ x^{-b}$" when drawn on a log–log plot turns out to be a straight line where "a" equals the intercept when "x" equals unity, and "b" is the slope of the line. The values of "a" above are given in ohms and "f" is the frequency in cps. All of the data seemed to fit this type of relationship quite well.

The reactance of a fixed value capacitor is given as follows:

$$x = \frac{1}{2\pi fc}$$

This can be written as follows:

$$x = \frac{f^{-1}}{2\pi c};$$

hence, it can be seen that if tissues act at any time as a true capacitor, the slope of the line will be equal to minus unity. The highest slope obtained in the present work was 0.56; therefore, our initial assumption that the capacitance changes with frequency is borne out.

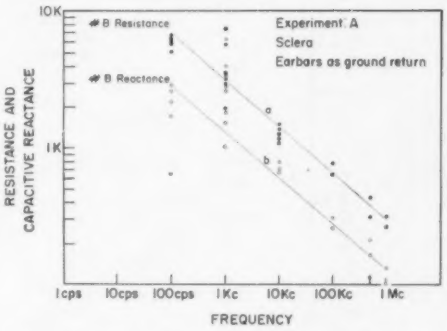


Fig. 2 (Knoll). Resistance and capacitive reactance of the sclera as a function of frequency, measured by the phase angle method. Electrode No. B was held against the sclera by a clamp (electrode holder not used). Ground obtained through ear bars. The lines represent the relationships expressed as a power function.

The sloping resistance line also bears out the assumption that the resistance changes with frequency.

Comparison of Flat and Pointed Electrodes

Using the Twin-T Impedance Bridge Method, the impedance of the flat electrode (No. B) was compared with the impedance of the pointed electrode (No. A) on the sclera. No electrode holder was used. The

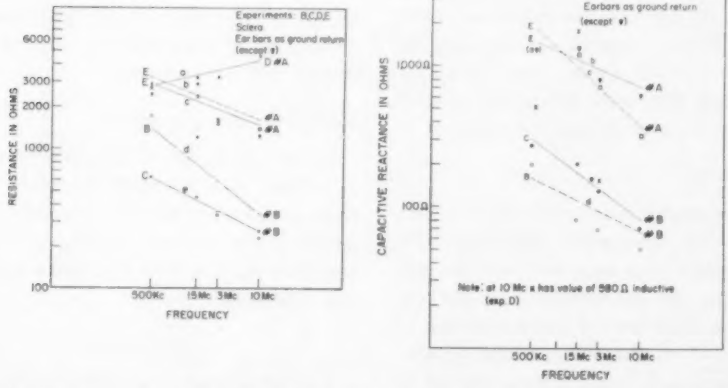
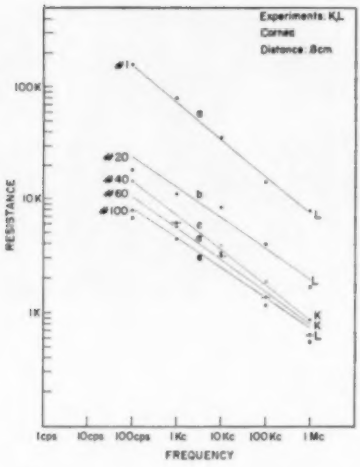
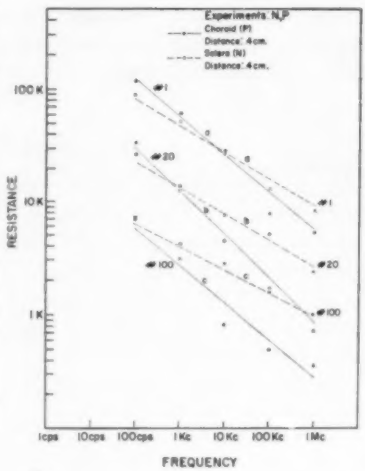


Fig. 3 (Knoll). Comparison of the flat (No. B) and the pointed (No. A) electrodes. Measurements made using the Twin-T Impedance Bridge Method. Each point represents an average of 10 readings. The conflicting data shown for Experiment D may be explained by excessive drying of the sclera.



4



5

Figs. 4 and 5 (Knoll). (Fig. 4) Electrode area effect shown using approximate method of measurement. (Fig. 5) Electrode area effects on choroid and sclera.

ear bars were used as the ground electrodes except during one experiment when the ground electrode was placed in the conjunctival sac. The results are shown in Figure 3. The resistance and the capacitive reactance values are lower for the larger flat electrode. One experiment (D) yielded conflicting data, which may be explained by excessive drying of the sclera.

Each point in Figure 3 represents an average of 10 readings. The scatter of points was taken to indicate the need for better electrode contact control. Hence, at this point the electrode holder was built, and the remaining data were taken with a much more uniform electrode pressure control.

Area effects

Using the approximate method, the effects of the electrode area were determined. The electrode holder was used to place the electrodes on the eye at separations of 8.0 mm. and 4.0 mm. In Figure 4 are shown the results as found on the corneas with an electrode spacing of 8.0 mm. The slopes of the lines are essentially the same, resistance being inversely proportional to the area. Figure 5 shows the results of choroid and sclera with an electrode spacing of 4.0 mm. The slopes of the lines for the various tissues seem to vary.

Postdiathermy effects

Using the No. 1 electrodes, 4.0 mm. apart, the impedances were measured before and after treatment with a Walker diathermy unit. The results are shown in Figure 6. Note particularly the increased slope of the capacitive reactance curve following treatment. This could be explained by the destruction of cell membranes.

Various tissue effects

In one of the previous reports,[1] the effect of cellular density upon impedance seemed to be a direct proportion. Results, using the phase angle method shown in Figure 7, bear this out for both resistance and capacitive reactance.

Discussion

The amount of power absorbed in an electric circuit is inversely proportional to the resistance in the circuit, provided the volt-

age is kept constant. The data presented here would indicate that for a series of oscillators having the same voltage with different frequencies, the amount of heat produced in the tissues would be inversely proportional to the frequency. At a given frequency the amount of heat absorbed would be greatest in the vitreous, less in the choroid, and least in the cornea and sclera (fig. 7). It can be seen that in surface diathermy it is fortunate that the flux density is higher in the outer coats of the eye and least in the choroid and vitreous. This leads to more intense heating in the outer layer of the eyes with relatively less heat dissipated in the choroid and vitreous. These observations lead to the further conclusion that one must be very careful when puncturing the coats of the eyeball, since the procedure leads to higher flux densities internally, which will lead to intense heating of the choroid, retina, and vitreous.

A most difficult problem, which eludes solution at this time, is the measurement of the electrical parameters during the time of treatment. Observations during the various experiments lead us to believe that the impedances drop during the treatment and may serve to heat all tissues to a much greater extent than would be indicated by the measurements recorded here.

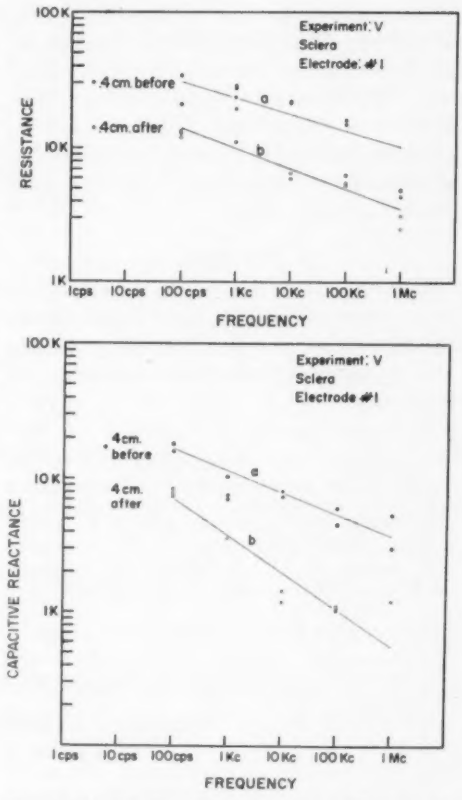


Fig. 6 (Knoll). Postdiathermy effects. Phase-angle method.

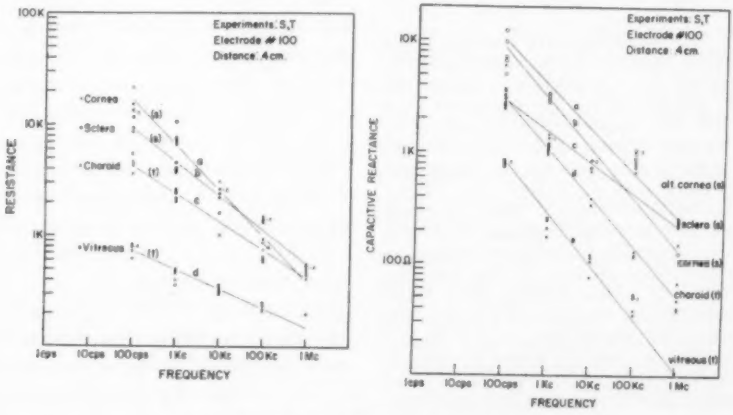


Fig. 7 (Knoll). The effects on various tissues.

Enough data are now available to enable at least close approximations to the amount of heat absorbed by ocular tissues when treated by means of tube-generated currents. It is to be hoped that equipment will be made available using this type of generation, to replace the spark gap equipment now being so widely used.

Summary

1. Using two methods of measuring the components of ocular tissue impedance, it has been established that both the resistance and capacitive reactance vary inversely with frequency.

2. The effect of electrode separation seems to be minor in relation to other factors such as electrode size, pressure, and dryness of the tissues.

3. The impedance is inversely proportional to the area of the electrode.

4. The impedance varies inversely with the cellular density of the tissue.

Acknowledgments

I wish to acknowledge the skillful assistance of Mr. Harvey Kirk and Mr. Stanley Polsky who assisted ably in carrying out the experiments. Without their assistance the performance of the experiments would not have been possible.

References

1. Knoll, H. A.: An experimental investigation of the basic phenomena of retinopexy: I. Electrical impedance measurements. Am. J. Ophth., **45**:546, 1958.

2. Schwan, H. P., and Carstensen, E. L.: Dielectric properties of the membrane of lysed erythrocytes. Science, **125**:985, 1957.

3. Sinclair, D. B.: The Twin-T: A new type of null instrument for measuring impedance at frequencies up to 30 megacycles. Proc. Inst. Radio Engineers, **28**:310, 1940.

THE USE OF ABSORBABLE SUTURES IN SURGERY OF THE CORNEA*

Samuel D. McPherson, Jr., M.D.
Durham, North Carolina

The choice of the most satisfactory suture material for corneal surgery is a controversial subject. The routine use of nonabsorbable sutures has been generally accepted, and the use of absorbable sutures has received little attention. Absorbable suture materials offer a definite advantage in the closure of clear corneal wounds because they do not have to be removed. The removal of corneal sutures is frequently a hazardous procedure and may result in loss of the anterior chamber, wound separation or disruption, or occasionally dislocation of a corneal graft. In children the removal of nonabsorbable sutures usually necessitates a second general anesthetic. Most of these difficulties may be obviated by the use of sutures which are absorbable and do not require removal.

In spite of the common use of catgut sutures in general surgery and in certain types of ocular surgery, the use of similar sutures for corneal surgery has not been widely advocated. The general impression seems to be that the use of absorbable sutures for the closure of corneal wounds may produce un-

* From the McPherson Hospital, Durham, North Carolina and the Division of Ophthalmology, University of North Carolina School of Medicine, Chapel Hill, North Carolina. The operations were performed with the assistance of the resident staffs of the McPherson Hospital and North Carolina Memorial Hospital. The experimental work was done in the Laboratory of Experimental Ocular Pathology of the University of North Carolina with the assistance of J. W. Draheim, M.D., and G. T. Kiffney, Jr., M.D., Histologic sections were prepared by Mrs. Vivian Sparks. The experimental studies were aided by a grant from the North Carolina Association for the Blind, and the materials in the experimental portion of this paper were furnished by the Ethicon Suture Company, Somerville, New Jersey. Candidate's thesis submitted for membership and published in the Tr. Am. Ophth. Soc., 1959, v. 57.

predictable wound healing and excite more tissue reaction than usually occurs with silk or other nonabsorbable materials.

It is the purpose of this paper to examine the historical background and to report the experimental findings and clinical use of plain and chromic catgut sutures in surgery of the cornea.

Historical

The use of sutures for wound approximation is one of the oldest surgical techniques, and sutures which are of animal origin are among those first mentioned. The Edwin Smith Surgical Papyrus,[1] written in the 17th century B.C., is thought to have originated in the pyramid age (3000-2500 B.C.) and to be the oldest surgical reference in existence. Prof. James Henry Breasted, its translator, says that surgical stitching is mentioned for the first time when the author states, "Thou wouldst draw together for him his gash with stitching."[2]

Susruta,[2] the Hindu surgeon (500 B.C.), noted that suture materials should be of cotton, hemp, leather, horsehair or animal sinews. Hippocrates[2] (400 B.C.) preferred wound healing by first intention and drew the edges of wounds together with sutures. Galen[2] (150 A.D.) wrote a short dissertation on ligatures. In it, he discussed linen, silk, and thin gut strings (gracilium chordarum). He recommended the latter because they "do not putrefy readily." Rhazes,[3] the Arabian surgeon (900 A.D.), mentioned the use of harp strings as suture material. At that time, harp strings were made of sheep intestine and were also used as fiddle strings for a three-stringed violin developed by the Arabs and known as a "kit." It is thought that this kitgut represents the origin of our modern term catgut.[4] It is not certain that ligatures and sutures were prepared from animal tissues because of their absorbable qualities since many ties and threads of that time were made from animal hides and sinews.

During the late middle ages, surgery fell into disrepute, and little mention is found in the surgical literature of sutures and ligatures. In the late 18th century, Phillip Syng Physik (1768-1831),[5] one of John Hunter's favorite American pupils, began to evaluate various suture materials in an attempt to find some substances which would be absorbed and would not slough. Among the material which he used were buckstring, French kid and animal gut.

The present-day use of absorbable sutures actually begins with the work of Joseph Lister[5,6] in 1867. For several years prior to that time, Lister had devoted himself to the study of Pasteur's papers on micro-organisms as the cause of wound putrefaction and in 1867 published a paper entitled "On a new method of treating compound fracture, abscess, etc., with observations on the conditions of suppuration." This is generally regarded as the first attempt at aseptic surgery.

As a part of his work in wound asepsis, Lister attempted to prepare sutures which might be sterile and absorbable and therefore would not slough. At that time the common ligature used was waxed silk. When an artery was ligated, the ends of the silk ligature were cut long and allowed to protrude from the wound. Several days after operation, the sutures sloughed from retrograde infection and were simply pulled out. Not infrequently, the ligated vessel began to bleed, and severe secondary hemorrhage occurred. To prevent this occurrence, Lister soaked his silk sutures in carbolic acid prior to using them. The sutures could then be cut short and buried in the wound without retrograde infection or delayed hemorrhage. It soon became evident that silk was a difficult material to sterilize in this manner, and shortly thereafter Lister began to prepare catgut in a similar manner. In 1869 carbolized catgut first became available as a sterile absorbable ligature and suture.

Subsequently, absorbable sutures were prepared from the intestinal tissues of sheep and cattle, from the tendons of ox, kanga-

roo, rat, whale, raccoon, and from the fascia lata of humans. These materials were tanned with mercury, thymol, carbolic acid, silver, formaldehyde, tannic and chromic acid.[7,8] For the next 40 years these various absorbable sutures were used by general surgeons with an apparent high incidence of wound infection. Dissatisfaction with any single absorbable suture material is indicated only by the variety of sutures proposed for there was little written in the medical literature of that time proposing a return to nonabsorbable sutures.

In 1913 Halsted[9] published an article on ligature and suture materials in which he condemned the use of catgut for any purpose in clean surgical wounds. Halsted stated that he abandoned catgut in 1883 and had not used it since. He listed six objections to catgut. They were: (1) the high cost of catgut; (2) its bulky size; (3) the inconvenience of its use and sterilization; (4) its inadequacy in wound closure; (5) its uncertain time of absorption; and (6) the reaction it excites. This article had a profound influence on general surgeons throughout America and until this day most surgeons of the Halsted school prefer to use sutures or ligatures of silk.

Since Halsted's time, the argument of absorbable versus nonabsorbable sutures has continued. In 1932, Marchesani[10] demonstrated hyperemia, edema, leukocytic infiltration and local necrosis around catgut sutures introduced into animals previously sensitized to catgut by subcutaneous injection of a catgut extract. He stated that these animals gave a positive ophthalmic reaction and that systemic hypersensitivity could be produced by the introduction of catgut extract into the conjunctival cul-de-sac.

Frugoni[11] found that animals sensitized in this manner failed to produce precipitins and questioned the production of a true hypersensitive state.

Kraissl, Kesten and Cimiotti[12] were able to sensitize rabbits to plain catgut, chromic catgut and chromic acid. Sensitivity was routinely produced within three weeks as tested by intradermal injection. The sensitized animals were laparotomized and the incisions closed with the appropriate suture material. The sensitized animals showed a much higher incidence of wound disruption than did a similar group of nonsensitized animals. They further reported a series of patients sensitive to catgut who at operation manifested a much higher incidence of suture complications than did a control nonsensitive group of patients.

In 1933 Erdmann[13] noted that, in patients with chronic disease and anemia, protein hunger frequently resulted in the digestion of catgut sutures before firm union occurred. Later Thompson, Ravdin, Rhoads and Frank[14] demonstrated in dogs that a decline in tensile strength of catgut was accelerated by the induction of hypoproteinemia.

In 1940, Meleney[15] reported that of 174 specimens of catgut purchased throughout the country, 22 were bacteriologically contaminated. These represented eight products of 18 firms. His findings were largely responsible for bringing absorbable sutures under the Pure Foods and Drugs Act in the following year. Effective July 1, 1941, catgut was considered a medicine and made to conform to the specifications of the *U. S. Pharmacopeia*.[16]

In 1943, Localio, Casale, and Hinton[17–19] studied the effectiveness of the now standardized catgut in the closure of laparotomy wounds in rats. They tested wound strength by inflating the peritoneal cavity with air until rupture occurred. They found no difference in the tensile strength of wounds repaired with plain and chromic catgut during the five-day lag period of healing. They did find a lesser tensile strength of wounds repaired with catgut during this period than in wounds repaired with cotton, silk, wire or nylon. Further, the lag period prior to increase in wound tensile strength and the healing period were longer with catgut than

with other nonabsorbable suture materials. Bacteriologic studies showed that wounds repaired with catgut had a much higher incidence of contamination than did wounds repaired with nonabsorbable sutures. Pathologic studies of similar wounds demonstrated that catgut produced a serous reaction for nine days with the formation of a fibrinopurulent membrane between the second and seventh day. Wound edema persisted for a longer time than with nonabsorbable materials, and maturation of fibroblasts and collagen formation were delayed. Fragments of catgut surrounded by a zone of inflammatory reaction were present after two months. Wounds sutured with nonabsorbable materials showed little serous reaction, and edema disappeared more quickly. At two months, the nonabsorbable material was still present but was fragmented and encapsulated by fibroblasts with less surrounding inflammatory reaction.

Madsen[20-22] studied the histologic picture of suture materials in rabbits and in man. He concluded that the reactions were so similar that the rabbit was an ideal laboratory animal for the study of sutures. The only discrepancy noted was that catgut tended to absorb more quickly in man. He found that with plain catgut there was a marked exudative tissue reaction with delayed formation of collagen. Knots tended to slip, and the material was not considered reliable for closure of fascial wounds. The finer, nonabsorbable suture materials showed minimal tissue reactions and retained their initial tensile strength. The knots were considered safe. Chromic catgut seemed to represent a compromise. The exudative reaction was moderate, and there was prolonged holding power of the thread with greater stability of the knot. He investigated 1,211 patients in whom plain catgut, chromic catgut or nonabsorbable suture materials had been used. He found all types of suture complications except suture extrusion to be less common with nonabsorbable sutures.

In cataract surgery

The first investigations of the use of catgut sutures in cataract surgery came in 1943 following the standardization of catgut by the Food and Drug administration and its inclusion in the *U. S. Pharmacopeia*.[16]

Hughes[23] and Hughes, Guy, and Romaine[24] reported the clinical and experimental use of catgut in the closure of cataract incisions. They found that in experimental animals no suture held the corneoscleral wound closed after the fifth or seventh postoperative day. Absorbable sutures were found to produce more tissue reaction than nonabsorbable sutures for the first three postoperative days. Five-0 plain catgut held the wound in approximation for five days and was absorbed at 15 days. Five-0 mild chromic catgut held the wound edges in approximation for a longer period of time but caused an objectionable tissue reaction. The suture materials investigated were nylon, 3-0 plain catgut, 3-0 mild chromic catgut, 5-0 mild chromic catgut and 5-0 plain catgut. The authors concluded that 5-0 plain catgut was the most ideal material for closing cataract wounds in experimental animals and in the patients operated.

Guy,[23] in a discussion of Hughes' paper, pointed out that one still must consider Halsted's objections to catgut and Meleney's findings of contamination. He stated that he felt, however, that 5-0 plain catgut as used in cataract surgery by Hughes has adequately answered Halsted's objections.

Davis,[25] in 1944, reported the use of 5-0 plain catgut corneoscleral sutures in more than 70 operations and stated that he had no complication except for an occasional anterior chamber hemorrhage. Alger[26] reported a similar series of cases in 1947 and stated that he had no suture complication in 76 operations except for one anterior chamber hemorrhage. In 1950, Davis[27] compared the clinical results of the use of silk and catgut in the closure of cataract incisions. Although he could demonstrate no statistical differ-

ence in the outcome, he felt that silk was superior for the closure of cataract incisions.

Fralick[28] in 1950, reported the use of 6-0 mild chromic catgut in the closure of cataract wounds and stated that he felt any fine suture material which afforded wound closure for five to seven days was suitable. He noted a four-day lag in the onset of wound healing and attributed this to increased steroid secretion from surgical shock.

Dunnington and Regan,[29,30] in 1951, studied the effects of silk, catgut and thrombin upon ocular wound healing in monkeys. They found that thrombin interfered with wound healing by preventing apposition of the wound edges. With silk, tissue necrosis and epithelial downgrowth along the suture tracks were the outstanding reactions. Neither of these undesirable features was present with plain or mildly chromicized catgut. With either type of catgut, a polymorphonuclear cell reaction occurred which was earlier and more pronounced with plain than with mildly chromicized catgut. This reaction led to suture fragmentation which began to occur at the seventh postoperative day with chromic catgut. Fibroblastic proliferation and vascularization began to occur at the fifth day and increased until the 14th day, yielding a wound which was broader and more vascularized than that occurring with silk. In spite of this, the authors felt that the wound healing was equal to that obtained with silk and recommended its use for the closure of cataract incisions.

Subsequently, clinical reports have been published by Taylor[31] in 1952, Roberts[32] in 1952, and Stocker[33] in 1956, of the use of chromic catgut sutures in the closure of cataract incisions. All stressed the advantage of not having to remove sutures and the relatively low incidence of postoperative complications. Stocker[34] in 1957 reported the use of 6-0 plain catgut sutures for the same purpose and stated that, although he had not followed the patients for a long period of time, the results were encouraging.

In corneal surgery

All of the studies reported to this point have dealt with the use of catgut sutures in corneal wounds placed at the limbus where not only the avascular cornea was involved but also the vascular sclera and conjunctiva. The first reference to the use of catgut sutures in the repair of wounds in clear cornea is by Fralick[35] in 1952. In reporting the use of mildly chromicized catgut sutures for the closure of cataract incisions, he stated that some had used the same material in the repair of corneal and scleral lacerations.

Kirby,[36] in 1954, reported the use of mildly chromicized catgut sutures in two cases of penetrating keratoplasty. He used multiple direct sutures with tissue bites of approximately one mm. and recommended that the ends of the sutures be cut two to three mm. long. The sutures disappeared in from 10 to 20 days, and the outcome was said to have been good in both cases.

Paton,[37] in 1955, mentioned that 6-0 mild chromic catgut is less satisfactory than silk in penetrating keratoplasty. He found the sutures to dissolve slowly, particularly the knots, some of which were still present three weeks after operation.

Recently Kronenberg[38] reviewed the present status of ocular sutures but made no reference to the use of absorbable sutures in the repair of clear corneal wounds.

Preparation of modern catgut

Catgut as it is presently available is prepared from the intestine of sheep.[39–41] The small intestine is removed in an abbatoir and quickly frozen and stored. When the material is needed, the intestine is removed, thawed and, by a mechanical process, the mucosa, muscularis, and serosal layers are removed, leaving only submucosa which is composed almost entirely of collagen fibers. The submucosa is cut into longitudinal ribbons, and from one to six of these ribbons are spun or twisted together to form a uniform strand under tension. The strands are

polished and cut to appropriate size and, in this form, the raw catgut suture material is prepared. The strands are then thoroughly dried with heat. It is important that the drying is complete. If water is allowed to remain in contact with catgut throughout the period of storage, proteolysis will occur with swelling of the material and a subsequent loss of tensile strength.

Two means of tanning raw catgut with chromic oxide are available. The first technique is referred to as ribbon chromicizing and the second, string chromicizing. In ribbon chromicizing, the individual ribbons of catgut are treated with chromic oxide prior to being twisted together. This is said to afford an even distribution of the chromic oxide throughout the suture substance and to give an even rate of absorption of the entire suture. With string chromicizing, the suture is not treated until after the ribbons have been twisted together. String chromicizing is said to give rise to an uneven distribution of chromic oxide throughout the substance of the suture and therefore an uneven rate of absorption, with spotty loss of tensile strength at different points throughout the length of the suture. An even distribution of chromic oxide is necessary for a predictable delay in the rate of suture disappearance. The suture, either plain or chromicized, is then regauged for size. Tensile strength is again rechecked prior to sterilization and packaging.

At the present time, most catgut sutures are sterilized by exposure to high temperature, although sterilization by an electron beam has been proposed to retain a higher tensile strength of sutures.[42] The sutures are prepared and tubed as either boilable or nonboilable, plain or chromic catgut.

Boilable catgut is sealed in a glass tube containing xylol. The suture is sterilized with heat. The exterior of such a tube may be sterilized by boiling or autoclaving or storage in a sterilizing solution of alcohol and formaldehyde. However, when a tube is opened, the catgut is frequently stiff and must be softened prior to use. Boilable catgut is said to be consistently weaker than nonboilable catgut when removed from the tube. Softening by soaking in sterile water or in saline further weakens boilable catgut. Most surgeons prefer nonboilable catgut since its tensile strength is more predictable at the time of operation.

With nonboilable catgut, the suture is sealed in a glass tube containing a mixture of alcohol and water. This mixture has a plasticizing effect on catgut and renders a suture which is soft, pliable and ready for use as soon as the tube is opened. If such a tube is boiled, the water and alcohol will ruin the suture contained in it. Tubes of nonboilable suture materials must be kept totally immersed in a mixture of alcohol plus some antiseptic such as formaldehyde. When the sutures are ready for use, the

TABLE 1

SPECIFIED DIAMETERS AND TENSILE STRENGTHS OF ABSORBABLE SUTURES

Size	Diameter of Absorbable Surgical Suture				Mimimum Tensile Stength of Absorbable Surgical Suture Avoirdupois Pounds	
	Boilable Millimeter		Non-Boilable Millimeter			
	Min.	Max.	Min.	Max.	On Straight Pull	Over a Surgeon's Knot
0000000, 7–0	0.025	0.051	0.025	0.064	0.25	0.125
000000, 6–0	0.051	0.102	0.064	0.113	0.5	0.25
00000, 5–0	0.102	0.152	0.113	0.179	1.0	0.5
0000, 4–0	0.152	0.203	0.179	0.241	2.0	1.0
000, 3–0	0.203	0.254	0.241	0.318	3.0	2.0

tube is removed from solution, placed on the operating table and opened at that point. The sutures are then ready for immediate use and do not require moistening although they may be dipped in sterile saline to remove the sterilizing solution if the surgeon so desires.

At the present time, suture manufacturers perform routine tests for sterility, tensile strength and diameter on each batch of sutures produced. The diameter and strength requirements for absorbable surgical sutures are specified in the *U. S. Pharmacopeia* and are reproduced in Table 1. The most commonly used ophthalmic catgut suture for intraocular surgery is 6-0 plain or chromic catgut. Its minimum diameter is 0.06 mm. and its maximum diameter is 0.113 mm. Its minimal tensile strength on straight pull is 0.5 avoirdupois pounds and over a surgeon's knot 0.25 avoirdupois pounds.

Formerly, catgut was described as 10-day, 20-day, or 40-day catgut. This was to designate the amount of treatment with chromic oxide and therefore the expected rate of absorption in normal tissues. Such a marked variation was found in tissue response to catgut designated in this manner that catgut is now designated by its resistance to certain tissue enzymes as being type A, plain or untreated, type B, with mild treatment, type C, with medium treatment, and type D with prolonged treatment. All are treated with chromic oxide.

Present day catgut is available either as ligature material with no needles attached or as suture material with needles swaged on, in which case the end of the catgut is screwed into the butt end of the needle to yield an atraumatic suture. With this suture, no knot or reflection of the suture is present at the point at which the catgut attaches to the needle. This type of suture has been most popular in ophthalmic surgery in recent years.

Experimental

The following investigations were undertaken to resolve some of the questions associated with the use of catgut sutures in corneal surgery.

I. Sterility of catgut

The first experiment was undertaken to determine the sterility of catgut sutures in routine use in clinical surgery.

During the course of intraocular surgery, 40 tubes of nonboilable 6-0 plain and medium chromic catgut were opened in the operating room under sterile conditions. The sutures were removed, and one quarter inch of suture was excised from the middle loop of the suture material. This was dropped into a sterile test tube, and this closed with a sterile cotton plug. The test tubes were taken to the laboratory, and 5.0 cc. of fluid thioglycolate media was added to the test tube containing the excised portion of suture. Cultures were incubated for five days at 37.5°C. and were examined daily for evidence of growth. Smears were then made from the thioglycolate media, and these were stained with Gram's stain. In the 40 sutures cultured, no organisms were found. Every fourth culture was subcultured on the third day to a blood agar plate which was incubated for three days at 37.5°C. No organisms were found in the subcultures.

Comment. The negative cultures of sutures in their day to day use in clinical surgery is the best means of demonstrating that sterility of catgut can now be routinely expected. Since Meleney's[12] work in demonstrating the high incidence of bacterial contamination in commercially prepared catgut, the *U. S. Pharmacopeia* has required testing of batches of sutures. This is far removed from the individual testing of sutures for sterility but represents a marked improvement in the standardization of sutures and, judging from the results of these cultures, represents an adequate test of sterility.

II. Reaction of rabbits' corneas to various suture materials

The following experiment was undertaken to determine the reaction of rabbits' corneas

to plain catgut, chromic catgut and silk sutures.

Adult rabbits of an average body weight of approximately 3,000 gm. were used for these experiments. The rabbits were anesthetized with intravenous sodium nembutal, and the hair around the lids of one eye was closely clipped. The eye was irrigated with a solution of sterile saline, and two drops of one-half percent tetracaine hydrochloride were instilled. The lids were draped with sterile gauze squares, and a five-mm. perpendicular incision was made with a keratome directly in the center of the cornea. One suture each of 6-0 plain catgut, 6-0 medium chromic catgut and 6-0 silk was inserted. The sutures were placed half through the depth of the cornea, tissue bites of approximately one mm. being taken on each side of the wound. All sutures were tied triply (fig. 1). The animals were then returned to their cages.

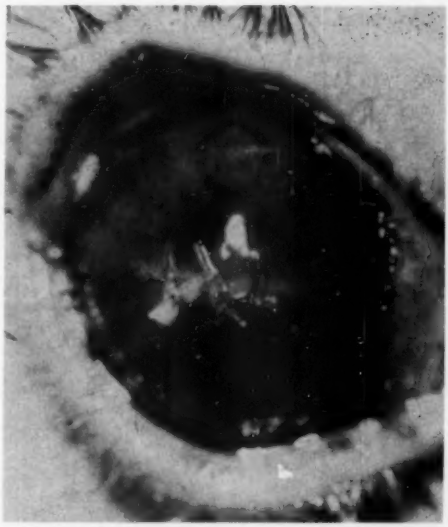


Fig. 1 (McPherson). Technique for closing corneal incisions in rabbits. From left to right suture materials are 6-0 plain catgut, 6-0 medium chromic catgut, and 6-0 silk. Photograph taken one week after operation.

Ten animals were used for these experiments, and two animals were killed at periods of 4, 8, 11, 18 and 28 days after operation. The operated eye was removed and placed in 10-percent formalin. The eyes were imbedded in paraffin, sectioned, and stained with hematoxylin and eosin. Serial sections were examined for histologic changes in the vicinity of the three sutures; 400 sections were examined from each eye.

Observations. At four days sections showed marked corneal edema adjacent to the wound. There was epithelial invasion of the suture tracks of all three suture materials, in some instances lining half of the entire track. Portions of the cornea included in the suture showed moderate acellularity and necrosis. There was some slight infiltration of the cornea with mononuclear cells and polymorphonuclear leukocytes. There was no evidence of fibroblastic proliferation or suture fragmentation. There was no difference in the reaction around the three suture materials.

At eight days sections, in addition to the changes, already noted, showed epithelial lining of the suture track which was now pronounced with all three suture materials. It was noted that epithelization was most extensive on the outer side of the suture opposite the wound (fig. 2). Infiltration with polymorphonuclear leukocytes was more pronounced and proliferation of fibroblasts along the entire depth of the wound with plugging of the internal surface of the wound was evident (fig. 3). There was no evidence of suture fragmentation, and the reaction about the three suture materials was essentially the same.

At 11 days, there was a slight increase in the cellular infiltration about the sutures, and corneal edema was slightly less. Epithelial and fibroblastic proliferation were unchanged, and there was no apparent difference in the reaction to the three materials.

At 18 days sections showed a decrease in edema of the wound edges. Epithelization of the suture track, fibroblastic proliferation, and cellular invasion appeared unchanged. There was some fragmentation of catgut;

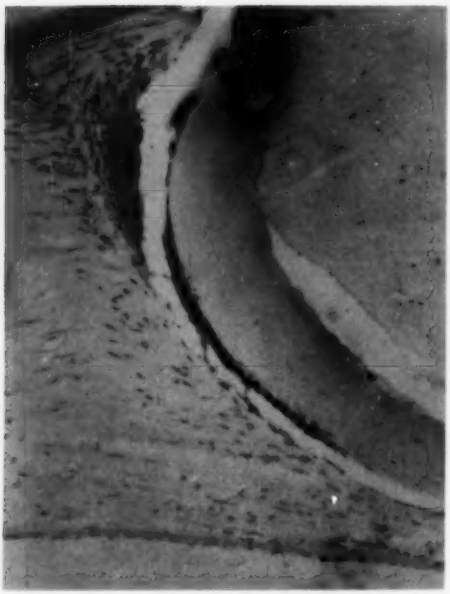


Fig. 2 (McPherson). Epithelization of suture track. Sections of rabbit's cornea eight days after repair with 6-0 medium chromic catgut, showing epithelization of most of the suture track on the side opposite the wound with necrosis of wound side of the cornea.

this appeared more pronounced with plain. There was no apparent difference in the reaction surrounding the three suture materials.

At 28 days corneal edema was markedly less. Epithelization of the suture tracks was now present only at the points where suture material persisted in the suture track. Proliferation of fibroblasts was unchanged, and the wounds appeared well sealed. Plain and chromic catgut sutures were fragmented, and there was marked phagocytosis of this suture material by polymorphonuclear leukocytes. This was more pronounced with plain than with chromic catgut (fig. 4). The surrounding cornea was infiltrated with polymorphonuclear cells. Necrosis of superficial corneal stroma was marked where suture knots remained, and therefore this was more frequently seen with silk than with catgut. Cellular infiltration of the cornea was more marked around silk than around plain or chromic catgut (fig. 5). Vascularization of the scar was not observed unless anterior synechias were present.

Comment. The results of these studies indicate that within 28 days there is little difference in the response of rabbits' corneas to suture materials of plain catgut, chromic catgut, and silk. The inflammatory response of the cornea to these materials occurred later than in tissues elsewhere in the body but, once it occurred, it had many of the characteristics reported in limbal tissue or fascia. The only differences noted in the present study were first, that there was little difference in the degree of necrosis or inflammatory cell response with any of the three suture materials and, second, that epithelization of the suture track was as

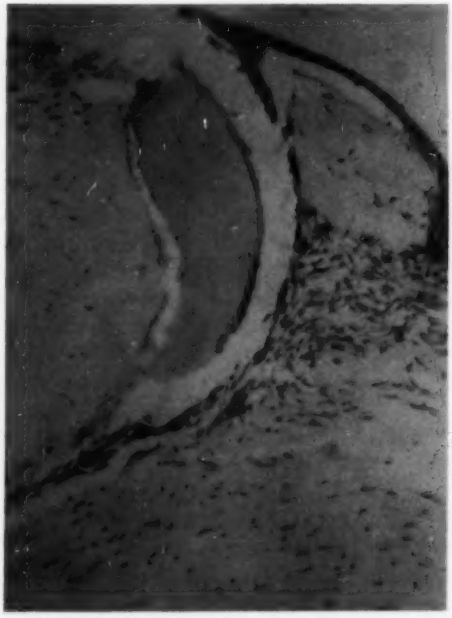


Fig. 3 (McPherson). Proliferation of fibroblasts and epithelization of suture track. Section of rabbit's cornea eight days after repair with 6-0 plain catgut, showing epithelization of suture track with an adjoining area of fibroblastic proliferation.

common with catgut as with silk. In contrast to this, Madsen[21] found that nonabsorbable suture materials produced less reaction than catgut in the abdominal wall of rabbits. Dunnington and Regan[29,30] found in monkeys that silk was more likely to produce tissue necrosis and epithelization of the suture track in limbal incisions. They also found the inflammatory response to be more pronounced to catgut than to silk and to occur at an earlier time.

The differences in tissue response noted by us and by Madsen and Dunnington and Regan are best explained by the differences in the tissues in which the sutures were placed. In the present experiment all sutures were placed in clear avascular cornea, and one would expect some delay in the onset of cellular infiltration and probably some diminution of the entire reaction. The lack of difference in response to various suture materials in the present study may be due to the fact that all three materials were used

Fig. 4 (McPherson). Phagocytosis of suture material. Sections of rabbit's cornea 28 days after repair with 6-0 medium chromic catgut suture, showing phagocytosis of suture material by polymorphonuclear leukocytes.

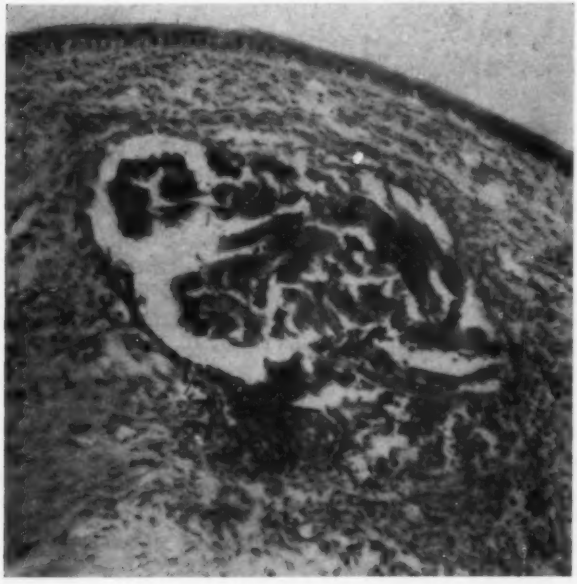


Fig. 5 (McPherson). Reaction to silk suture. Sections of rabbit's cornea 28 days after repair with 6-0 silk suture, showing dense cellular infiltration with polymorphonuclear leukocytes and proliferation of fibroblasts.

in the same wound in the same animal. This suggests that, to some extent, differences in reaction to suture materials in the cornea may be due to the individuality of response of any given animal and not to the differences in composition of various sutures.

The presence of epithelization of the suture track with catgut and silk in the present experiment is more difficult to explain. This may be due to the placement of all incisions in clear cornea where only corneal epithelium was involved. Dunnington and Regan placed their incisions at the limbus where transitional epithelium is present, and it is not unlikely that the growth characteristics of that epithelium are different.

III. Corneal reaction to suture materials in animals previously sensitized to catgut

The following experiment was undertaken to determine if the response of rabbits' corneas to catgut could be modified by sensitizing the animal to specific suture material prior to its use in closing corneal wounds.

Preparation of antigen. The antigen was prepared in a manner described by Kraissl, Kesten, and Cimiotti.[12] Ten milligrams of plain catgut were triturated by means of mortar and pestle until the gut was finely subdivided. This was then placed in a vial containing 10 cc. of 0.01 N sodium hydroxide and shaken in an aggigator for approximately eight hours. A suspension of gut was obtained in this manner. Five cc. of this suspension were placed in an autogenous vaccine bottle in a 56°C. water bath for two hours; 0.2 cc. were placed in 9.8 cc. of sterile physiologic saline containing 0.5-percent phenol as a bacteriostatic agent. An antigen of medium chromic catgut was prepared in a similar manner. These two types of antigens were used in these experiments. All solutions were cultured for contamination prior to use and found to be sterile.

Sensitization of animals. Adult rabbits weighing approximately 3,000 gm. were used for these experiments. Animals were sensitized to plain or chromic catgut in the following manner: 0.1 cc. of antigen was injected subcutaneously in the back twice weekly. Following the third injection, an area of skin was shaved and the animal skin-tested to 0.1 cc. of the same antigen. Animals routinely gave negative skin tests to control solutions, positive skin tests to catgut antigens, but negative ophthalmic reactions to both. When the animals had manifested two positive skin tests, they were considered to be sensitive for the purposes of this experiment. Most animals were found to be sensitive after the fourth subcutaneous injection. All animals received a minimum of seven subcutaneous injections prior to operation.

Animal operations were performed in approximately the same manner as described in Part II. If an animal had been previously sensitized to an extract of plain catgut, a corneal incision approximately four to five mm. in length was made, and this was closed with two sutures of a similar material. If the animal had been previously sensitized to chromic catgut, its incision was closed with chromic catgut sutures.

Ten animals were used for these experiments, and two animals were killed 6, 13, 20, and 28 days after operation. The operated eye was removed and fixed in 10-percent formalin. Eyes were imbedded in paraffin, sectioned, and stained with hematoxylin and eosin. Serial sections were examined for histologic change in the vicinity of the sutures; 400 sections were examined from each eye.

Observations. Histologic sections of these corneas showed changes which were quite similar to those seen in the previous series of animals which had not been sensitized.

Corneal edema was not marked at any time. Infiltration was mainly with polymorphonuclear leukocytes and occurred to a comparable degree and at a comparable time as in the previous experiment. There was no abundance of eosinophils and no pronounced wound necrosis. Nothing resembling an Arthus phenomenon was produced.

Epithelial invasion of the suture track regularly occurred at six days and subsided only when the suture material was no longer present in the track. Proliferation of fibroblasts was advanced by 13 days, and corneal incisions appeared well healed in 28 days.

In several eyes suture fragmentation was noted to be present at six and 13 days. This was sooner than had occurred in corneas of animals not previously sensitized. This was the only difference noted in the sections of these two groups of animals.

Comment. The failure to elicit an hypersensitive response in the cornea of animals previously sensitized to catgut may be due to many factors. The negative ophthalmic reactions combined with positive skin tests suggests that the hypersensitive state may have been a weak one. Catgut is composed almost entirely of collagen and is quite insoluble. The antigens used in the present study were suspensions and not solutions. This may explain the weak hypersensitive state or the negative ophthalmic reactions for it may be necessary to use a true solution to evoke a positive ophthalmic reaction.

Once the catgut sutures were placed in corneal tissue, their rate of digestion may have been so slow that they were not capable of evoking a hypersensitive reaction in this avascular tissue. The cornea may not possess antibodies in its central portion. The recent work of Germuth, et al.[43] suggests that corneal antibodies from systemic sensitization are present only in the peripheral cornea, and it may be that sutures placed in central cornea will not therefore produce an antigen-antibody reaction in the absence of corneal vascularization.

The entire subject of antigenicity of catgut has been recently re-evaluated by Van Winkle, Sewell and Wiland.[44] They were able to change the histologic picture of tissue response to catgut in experimental animals by sensitizing them to an antigen of catgut. In order to accomplish this, it was necessary to use an adjuvant of killed tubercle bacilli to increase the antigenicity of the catgut solution. It was their opinion that clinical sensitivity to catgut was quite unusual and probably represented a response to impurities contained in the suture material instead of a true collagen sensitivity.

The results of these investigations indicate the following:

1. That catgut sutures are now routinely sterile as prepared.

2. That in rabbits' corneas there is little difference in the reaction to plain catgut, chromic catgut, or silk in 28 days.

3. That this reaction is little modified in animals previously sensitized to catgut antigen.

Catgut sutures in the repair of corneal lacerations

Since January 1, 1956, we have used plain and chromic catgut sutures routinely in the repair of corneal lacerations. Initially, chromic gut was used in each case. When it became apparent that the sutures were remaining in place for prolonged periods of time, plain catgut was used.

Each patient suffered a laceration of clear cornea with or without iris prolapse and lens damage, and, in 26 patients, only clear cornea was involved in the suturing process. The records of these 26 patients were selected for analysis and are presented in Table 2. The youngest patient operated was two years of age and the oldest 54.

Surgical technique

In each case the patient was taken to the operating room on admission and with sterile technique the corneal wound was closed with interrupted sutures of the selected material. The sutures used in these operations were either 6-0 plain gut or 6-0 medium chromic catgut with swaged needles. The sutures were passed through half the thickness of the cornea, and, an attempt was made to include not less than one mm. of corneal tissue with each bite of the suture on each side of the wound. All sutures were tied triply. The remaining surgical repair was done in the

TABLE 2

CORNEAL LACERATIONS

Patient Identity	Age (yr.)	No. of Sutures	Time of Suture Disappearance (da.)	Vascularization of Suture Tracts	Complications	Result
					6–0 Plain Catgut	
171800	2	4	4 at 21		Anterior chamber hemorrhage 3rd postop. day	Scarring moderate, fundus well seen
166810	5	2	2 at 19		None	Scarring moderate, vision 20/60
170942	10	6	Present at 10			Enucleated on 10th postop. day for no light perception
170237	11	3	1 at 7 2 removed at 10	x	Anterior chamber lost when sutures removed	Scarring moderate, vision 20/60
166206	10	1	1 at 20		Developed traumatic cataract	Scarring moderate, vision 20/300
170101	3	2	2 at 16		None	Scarring minimal, fundus well seen
167850	4	8	6 at 18 1 at 25 1 at 38	x	Developed traumatic cataract	Scarring moderate, vision—light perception with projection
169600	6	3	3 at 5		Developed traumatic cataract with anterior synechia	Scarring moderate, vision light perception with projection
167474	54	1	1 at 12		Developed traumatic cataract	Scarring moderate, vision light perception with projection
					6–0 Plain Catgut	
165090	5	5	2 at 9 1 at 10 1 at 18 1 at 22		Developed traumatic cataract with anterior synechia	Scarring moderate, vision light perception with projection
					6–0 Chromic Catgut	
100691	33	1	1 at 13		Suture broke and removed at 13 days	Scarring minimal
173932	5	2	1 at 8 1 at 39	x	Much irritation from second suture	Scarring minimal
161904	53	3	1 at 20 1 at 29 1 at 34		Developed traumatic cataract and anterior synechia	Scarring moderate, vision light perception with projection
157500	2½	1	Not noted		Developed detached retina	Scarring minimal, vision light perception
165079	31	6	6 at 30	x	Developed traumatic cataract with anterior synechia	Scarring moderate, vision light perception with projection
159404	7	3	3 at 24	x	Developed traumatic cataract and detached retina	Scarring moderate, vision no light perception
					6–0 Chromic Catgut	
159667	41	3	Not noted		Developed phthisis bulbi	Scarring moderate, enucleated 50 days after repair
157954	17	3	3 at 25	x	Developed pain on 18th day from loose suture	Scarring moderate, vision 20/25+
155586	2	2	Present at 8		Course uncomplicated	No follow up

TABLE 2 (*Continued*)

Patient Identity	Age (yr.)	No. of Sutures	Time of Suture Disappearance (da.)	Vascularization of Suture Tracts	Complications	Result
158791	5	4	4 at 35	x	Healed well but reinjured eye 6 mo. later	Scarring marked, enucleated
05-36-22	53	3	3 at 40		Developed traumatic cataract Lens removed on ninth day without incident	Scarring moderate, vision 20/200
05-68-27	4	3	1 at 21 1 at 28 1 at 56	x	Developed anterior synechia	Scarring moderate, vision 20/40+
05-14-32	10	2	Present for 3		Developed endophthalmitis	Enucleated third postoperative day
06-74-62	6	4	4 at 17	x	Developed sympathetic ophthalmia—cleared on steroid therapy	Scarring minimal, vision 20/40
06-47-91	8	8	8 at 16		None	Scarring minimal, vision 20/40
05-07-17	5	3	Not noted	x	Developed phthisis bulbi	Scarring moderate, enucleated 11 months postoperatively

usual manner with iridectomy or lavage of the lens as indicated. The eyes were routinely dressed with an antibiotic and cycloplegic ophthalmic ointment with sterile dressings. Dressings were changed daily, and most patients were discharged from the hospital on the seventh postoperative day.

Postoperative course

In seven patients the postoperative course was uneventful. In four patients, enucleation was performed as a secondary procedure. One enucleation was done for purulent endophthalmitis on the third postoperative day, one for phthisis bulbi, one for a second injury six months later, and one because the patient lost all light perception on the 10th postoperative day.

Three patients complained of moderate irritation, presumably from the corneal sutures; however, healing was uneventful. In two patients one suture became untied and was removed. In six patients anterior synechias developed from the iris or lens capsule to the corneal wound. One patient developed an anterior chamber hemorrhage which cleared in 48 hours. With one patient, when removal of a suture was attempted because the suture ends seemed to lie directly in the corneal wound, the anterior chamber collapsed. This reformed in 24 hours with a pressure dressing, and healing was uneventful thereafter.

One patient developed sympathetic ophthalmia seven weeks after repair of a corneal laceration with iridectomy for iris prolapse. This cleared quickly with systemic and topical steroid therapy. Four months after the onset of sympathetic ophthalmia, both eyes were white and quiet. Vision in the exciting eye was 20/40 and in the sympathizing eye 20/15.

There was no instance of wound separation, iris prolapse or stitch abscess.

Observations

Of the 26 lacerations repaired, 10 were sutured with plain 6-0 catgut and 16 with 6-0 chromic catgut. Thirty-five plain catgut sutures were used, and 51 chromic were

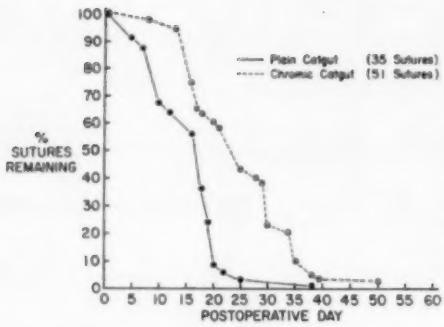


Fig. 6 (McPherson). Disappearance of plain and chromic catgut sutures in repair of corneal lacerations.

used. Of the 35 plain sutures used, the earliest time of disappearance* of the suture noted was five days after operation, and the longest noted was 38 days. The average time of disappearance of plain catgut sutures was 15.9 days.

Of the 51 chromic catgut sutures used in 16 lacerations, the earliest time of suture disappearance noted was eight days, and the longest noted was 56 days. The average time of disappearance of chromic catgut sutures was 25.7 days.

Ten of the 26 wounds became vascularized to some extent. Eight of the vascularized wounds occurred in eyes repaired with chromic catgut; two of the vascularized wounds occurred in eyes repaired with plain catgut. In the eight wounds repaired with chromic catgut in which vascularization occurred, 28 sutures were used, and the average time of disappearance was 28 days. In contrast to this, the eight wounds repaired with chromic catgut in which vascularization did not occur and in which 23 sutures were used, the average time of suture disappearance was 23 days. This suggests that the prolonged presence of sutures in the cornea may stimulate vascularization. Similarly, two of the vascularized wounds occurred in eyes repaired with plain catgut sutures. Eleven sutures were used in these wounds, and the average time of suture disappearance was 19.9 days. Eighteen plain catgut sutures were used to repair seven wounds which did not become vascularized. The average time of suture disappearance in those eyes was 14.9 days.

* The term disappearance is used to indicate absence of the extracorneal portion of the suture.

Comment

A comparison of the rate of disappearance of plain and chromic catgut sutures used in these operations is shown in Figure 6. Fifty percent of the plain catgut sutures disappeared in 17 days and 50 percent of the chromic in 26 days. The only obvious difference in the slope of the two curves is present in the first 10 days where there is a fall in the curve for plain catgut as contrasted with the plateau in the curve for chromic. This seems to indicate that the main effect of chromicizing is the delay in onset of suture deterioration. Otherwise, the curves for plain and chromic catgut are quite similar in shape. If the curve for chromic catgut were advanced 10 days, it would superimpose well over that for plain catgut, indicating that the degree of chromicizing obtained with this suture is sufficient to retard the disappearance of catgut by about 10 days.

The prolonged presence of sutures in corneas which became vascularized and the early disappearance of sutures in corneas which did not become vascularized suggests that the prolonged presence of catgut corneal sutures may serve as a stimulus to corneal vascularization. This is certainly true of other corneal foreign bodies and would be expected with any foreign substance that is present for a sufficient period of time. These figures indicate that, when sutures persist for more than three weeks, at least the extracorneal portion should be removed. In those patients in whom this portion of the suture was removed, irritation seemed to be immediately relieved. It was found that

removal of the entire suture was technically difficult, since the intracorneal portion of the suture was organized into the corneal stroma and would not slide through as easily as silk.

Topical steroid therapy seemed to have little effect on the vascularization of wounds repaired with catgut. More patients with vascularized corneas received steroid than did those without vascularized corneas. Steroid in those cases was given primarily to block postoperative uveitis and not to inhibit corneal vascularization.

Corneal scarring did not seem more pronounced in these patients than in those whom we had previously repaired with silk sutures (figs. 7 and 8). Of the 26 patients, five were noted to have minimal corneal scarring and 19 moderate corneal scarring. In two patients enucleation was done before corneal scarring could be evaluated.

A review of the literature reveals no report of clear corneal lacerations repaired with absorbable sutures. Snell[45] and Duke and Schimek[46] reported large series of perforating ocular injuries repaired with conjunctival flaps and direct fine silk sutures, and made no reference to the use of absorbable sutures. Snell reported that wound breakdown occurred in six of 38 cases repaired with direct silk sutures. Although no reference is made to the use of catgut sutures, he states that a conjunctival flap secured with catgut sutures may eliminate the necessity for a second general anesthetic in children.

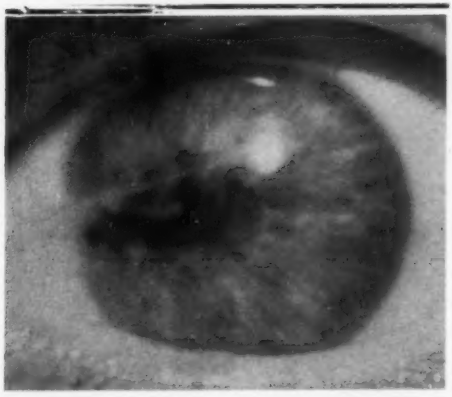


Fig. 7 (McPherson). Corneal scarring following repair of laceration. Six months after repair with 6-0 plain catgut, scarring considered minimal.

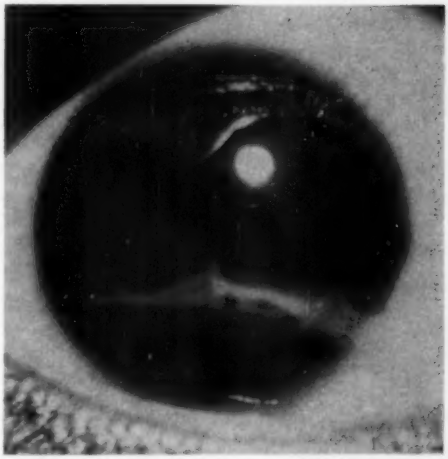


Fig. 8 (McPherson). Corneal scarring following repair of laceration. Six months after repair with 6-0 medium chromic catgut, scarring considered moderate.

The adequacy of catgut sutures in the present series is best indicated by the fact that there was no instance of wound separation or disruption. The only loss of anterior chamber came when suture removal was attempted.

Catgut sutures in keratoplasty

Since April 1, 1956, we have used plain and chromic catgut sutures in 11 keratoplasties in 10 patients. It was felt that a trial of catgut sutures was justified in these patients because they had a relatively poor prognosis for return of vision and required large grafts which would place the suture lines well away from the visual axes of the grafts. The records of these patients are summarized in Table 3.

Lamellar grafts were done on two patients and penetrating grafts on nine patients. The smallest graft done was eight mm., a lamellar graft, and the largest was 10 mm., a penetrating graft. One lamellar graft was

TABLE 3

KERATOPLASTIES

Patient Identity	Preoperative Diagnosis	Type of Graft	No. and Type of Sutures	Time of Suture Disappearance (da.)	Complications	Result
151773	Fuchs' dystrophy, nuclear cataract	9 mm. perforating	12 6–0 chromic	4 at 28 6 at 49 2 at 64	Vascularization of suture tracts, 2 sutures removed. Developed filtering bleb	Clear graft, vision 20/50 prior to cataract
163533	Keratoconus	9 mm. perforating	8 6–0 chromic	2 at 15 2 at 20 2 at 34 1 at 41 1 at 50	2 suture tracts vascularized, 1 suture untied, 1 anterior synechia; synechiotomy done	opaque graft, vision H. M. at 1′
163533	Opaque graft	10 mm. perforating	8 6–0 chromic	6 at 19 2 at 22	Late edema of graft, cleared with steroid	Graft partly clear, vision 20/50+
05-70-17	Vascularized, adherent leucoma	9 mm. perforating	8 6–0 plain	4 at 12 4 at 18	Graft vascularized	Graft partly clear, vision 3/200
04-26-22	Vascularized, adherent leucoma	9 mm. perforating	8 6–0 plain	6 at 15 2 at 30	4 suture tracts vascularized, recurrent edema of graft	Graft partly clear, vision 3/200
07-03-77	Vascularized corneal scar, complicated cataract	9 mm. perforating with cataract extraction	10 6–0	10 at 45	Uneventful healing	Graft clear, fundus lesion, vision hand movement
04-07-10	Opaque vascularized corneal graft, complicated cataract	9 mm. perforating	8 6–0 chromic	8 at 28	Healing uneventful	Graft clear, vision light perception due to cataract
155948	Atypical corneal dystrophy	10 mm. perforating with conjunctival flap	14 6–0 chromic	14 at 22	Persistent corneal edema	Graft partly clear, vision 3/200
130364	Opaque corneal graft	10 mm. perforating with cataract extraction and conjunctival flap	8 6–0 chromic	7 at 19 1 at 42	Persistent corneal edema	Graft partly clear, vision 5/200
05-64-90	Corneal scarring and vascularization from metaherpetic keratitis	8 mm. lamellar	8 6–0 plain	2 at 5 6 at 7	Graft became vascularized, opaque	Graft opaque, vision 5/200
164140	Corneal scarring and vascularization	9 mm. lamellar	8 6–0 plain	6 at 16 1 at 18 1 at 20	Slight corneal vascularization	Graft clear, vision 20/200

done for metaherpetic keratitis and one for corneal scarring and vascularization of unknown cause. Of the nine penetrating grafts, three were done for corneal opacities following unsuccessful grafts, three for corneal scarring and vascularization of unknown cause, one for keratoconus, one for Fuchs' dystrophy, and one for an unclassified corneal dystrophy.

SURGICAL TECHNIQUE

All operations were performed under local anesthesia with a modified Van Lint lid block and retrobulbar injection of two cc. of two-

percent xylocaine containing seven T.R. units of hyaluronidase. If the graft was to be lamellar, the area to be removed from the recipient cornea was outlined to the appropriate depth with a Castroviejo corneal trephine and dissected with a Gill knife. A similar plug of cornea was removed from the donor eye using the same trephine. The donor cornea was then sutured into place in the recipient cornea using eight interrupted sutures of either 6-0 plain or chromic catgut.

If the graft was to be penetrating, the donor eye was trephined with a Castroviejo trephine of the selected size. The corneal plug was removed, and two opposing sutures of 6-0 catgut were placed in the cornea. The donor plug was then placed in a capped glass weighing bottle containing the patient's serum. The recipient cornea was then trephined with the same trephine. Removal of the corneal plug from the recipient cornea was completed with Castroviejo corneal scissors. Three or four small peripheral iridotomies or iridectomies were then done. The donor plug was removed from the weighing bottle and sutured into place using the two preplaced sutures and as many additional sutures as were necessary. Suture bites of approximately one mm. of tissue were taken in both donor and recipient corneas, and all sutures were tied triply. The number of sutures used with either technique varied with the size of the graft and the type of approximation achieved. The fewest sutures used were eight and the most 14. In two instances, the lens was removed before the final sutures were tied and, in two instances, the suture line was covered with a conjunctival flap brought up in a purse string suture. A bubble of air was injected into the anterior chamber either through the edge of the graft or through a small peripheral opening made with a Ziegler knife. A subconjunctival solution of 0.2 cc. of a mixture of penicillin and streptomycin was injected and the eye dressed with neosporin and pilocarpine ointments. Dressings were changed daily, and most patients were discharged from the hospital on the 12th postoperative day.

Fig. 9 (McPherson). Suture remaining 64 days. Medium 6-0 chromic catgut suture remained in place by excising the extracorneal portion. There was little reaction to suture material.

Postoperative course

The postoperative course of all cases was without major complication. Several patients complained of foreign body sensation when the sutures remained in place for prolonged periods of time. Two sutures which remained in place for 64 days were removed for this reason (fig. 9). One suture came untied at 28 days and had to be removed (fig. 10). Except for these three instances, the sutures disappeared spontaneously.

Following operation, one patient developed an anterior synechia which required synechiotomy. This was thought to be due to a poorly fitting graft and not to the suture material used.

One patient developed a filtering bleb at the limbus. In this patient, a nine-mm. perforating graft was placed eccentrically, and one suture was brought through the limbus. The filtering bleb developed at the site of this suture (fig 11).

There was no instance of postoperative loss of the anterior chamber, wound disruption or iris prolapse. There was only one instance in which one edge of the graft was noted to bulge and that occurred in the patient who required synechiotomy.

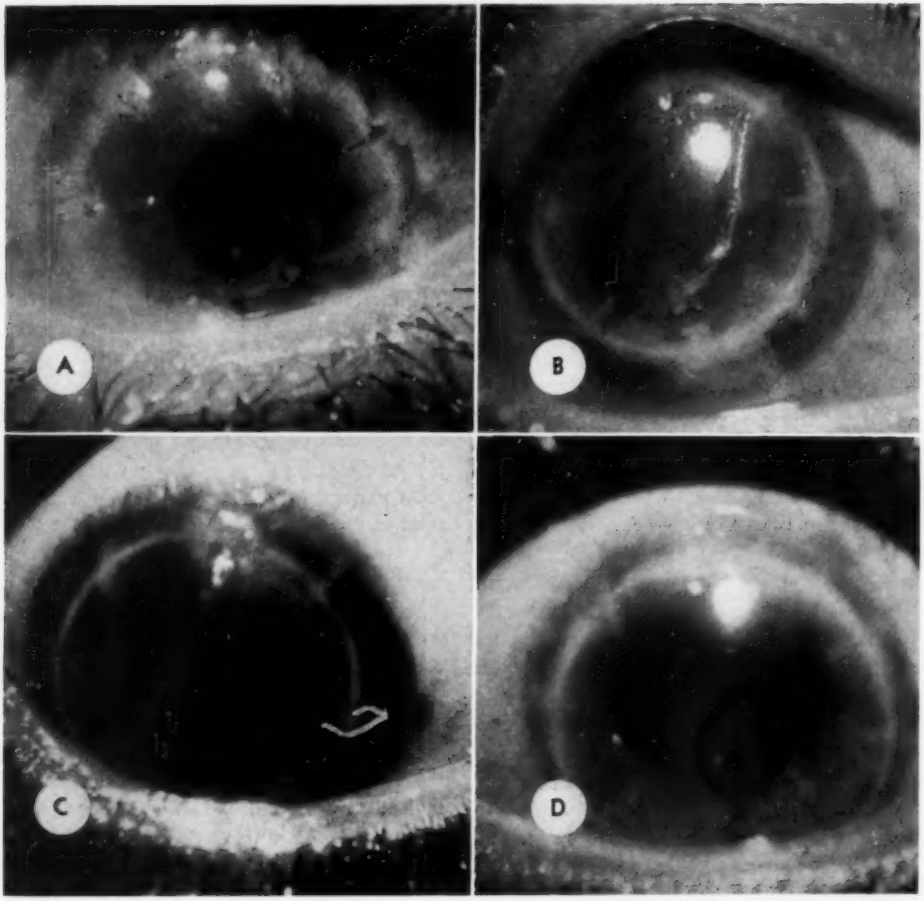


Fig. 10 (McPherson). Disappearance of sutures in a nine-mm. perforating graft. (A) Medium 6-0 chromic catgut sutures in place seven days after operation. (B) Suture which became untied at 28 days excoriating the cornea was removed. (C) A second suture remained in place for 50 days with little reaction. (D) All sutures have now been absorbed. The graft later became opaque necessitating reoperation.

Observations

In the two lamellar keratoplasties, eight 6-0 plain catgut sutures were used to secure the donor graft. In the nine penetrating keratoplasties done, 6-0 plain catgut was used in two operations, and 6-0 chromic catgut sutures were used in the remaining seven operations. Thirty-two plain and 68 chromic catgut sutures were used. The earliest time of disappearance of plain catgut sutures noted was five days, and the latest was 30 days. The average time of disappearance was 14.3 days.

Of the 68 chromic catgut sutures used, the earliest time of disappearance noted was 15 days, and the latest noted was 64 days. The average time of disappearance was 30.6 days.

In two patients who had previously avascular corneas, some vascularization of the suture tracks occurred (fig. 12). The remainder of the patients did not develop vascularization of the suture tracks unless cor-

neal vascularization was present prior to operation. There was no instance of vascularization of the corneal graft in its central portion in patients whose corneas were not vascularized prior to operation.

Comment

The rates of disappearance of plain and chromic catgut sutures are contrasted in figure 13. Fifty percent of the plain sutures disappeared in 16 days and 50 percent of the chromic sutures in 25 days. The immediate fall in the curve for plain catgut contrasts with the initial plateau for chromic catgut. Thereafter the slope of the two curves is similar and, if the curve for chromic catgut were displaced to the left by 10 days, it might be superimposed on that for plain catgut. As in the repair of corneal laceration, the curve for chromic catgut implies that the effects of chromicizing are manifested in delaying initial suture deterioration by about 10 days.

The effect of catgut sutures in promoting corneal vascularization could not be evaluated since several of these patients had corneas which were previously vascularized. All patients received topical steroid in the postoperative course and again the effect of steroid in blocking corneal vascularization or in delaying suture disappearance could not be assessed.

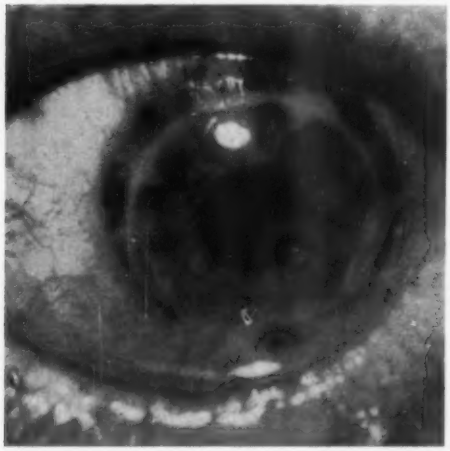


Fig. 11 (McPherson). Filtering bleb from suture at limbus. Medium 6-0 chromic catgut suture which penetrated the limbus was present where the filtering bleb has now formed.

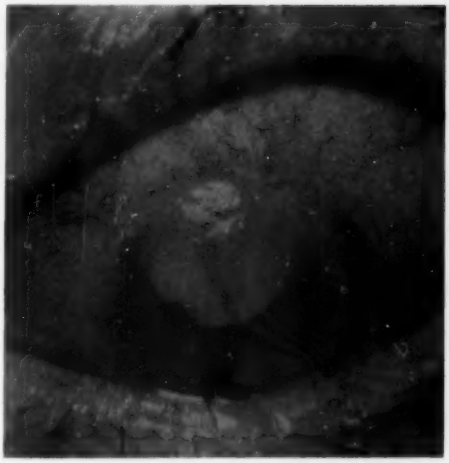


Fig. 12 (McPherson). Vascularization of suture track in previously avascular cornea. Plain 6-0 catgut sutures were used in this nine-mm. graft.

Wound healing was satisfactory in all cases. Postoperative scarring at the suture line and graft junction was not appreciably greater than we had encountered with other suture materials.

The visual results obtained were not good, but this might be expected from the selection of cases. Four grafts were considered to be clear postoperatively, five partially clear and two opaque. The failure to obtain a good

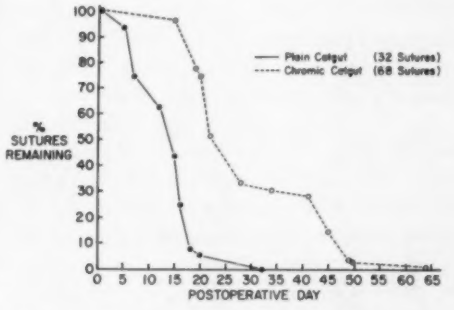


Fig. 13 (McPherson). Disappearance rates of plain and chromic catgut sutures in keratoplasty.

visual result or a clear graft seemed to be related to the type of disease present and not to the suture material used at operation.

Discussion

The ideal suture for corneal surgery should be:

1. Inexpensive and convenient to use.
2. Dependable as to sterility.
3. Reliable as to tensile strength and of the smallest diameter consistent with satisfactory function in a tissue exposed to the constant lavage of tears, the shearing motion of wound edges, the massage of the lids, and fluctuations of intraocular pressure.
4. Pliable, easy to handle and tie with a knot that is secure and stable.
5. So well tolerated by the host tissue as to reduce the chances of secondary infection, corneal scarring and vascularization.
6. Finally, since there are the well recognized hazards of infection, hemorrhage, and wound disruption inherent in the removal of nonabsorbable sutures, the ideal suture should undergo autolysis and absorption at a predictable rate.

These specifications are modifications of Halsted's postulates for an ideal suture with such additions as seem applicable to the problems of corneal surgery. Forty-five years ago his investigations led Halsted to the conclusion that silk most nearly approached the ideal suture material. While this opinion was not universally accepted, it had a marked influence on surgical technique. In fact, the reluctance of many American ophthalmic surgeons to accept catgut as suitable for corneal surgery may be the remote effect of Halsted's aversion to this material.

In intervening years, improvements in manufacture, standardization, sterilization and preservation of catgut sutures have gone far toward removing the characteristics of catgut sutures which were objectionable to Halsted. The cost of catgut sutures is now as reasonable as that of silk. Size and tensile strength are regulated by the *U.S. Pharmacopeia*. Sutures as now preserved are sterile when received. The adequacy of catgut in the closure of corneal incisions has been demonstrated in our hands, as evidenced by the closure of 37 corneal wounds with no single instance of wound disruption or separation. Only two of Halsted's original objections seem to remain valid to some extent.

There is still an uncertain time of absorption of catgut sutures. In the present study, plain catgut was found to disappear at some point between five and 38 days and chromic catgut between eight and 64 days. This wide variation in the time of suture disappearance is as difficult to explain here as it is in the general surgical use of catgut. Several explanations have been offered. Most explanations attribute failure not to any inconstancy of suture but to the peculiarities of the tissue in which it is placed. Protein hunger and catgut sensitivity are two examples of the many explanations that have been offered. In the closure of corneal wounds, we have observed that suture disappearance many times seemed to be the product of the size of the tissue bite. Therefore, the irregular time of suture disappearance on some occasions may be attributed to surgical technique.

Throughout this paper, the term disappearance has been used instead of absorption because, in many instances, the sutures sloughed instead of being absorbed. On some occasions the extracorneal portion of the suture sloughed away, the intracorneal portion varying in its later period of disintegration. In still other instances, the entire suture seemed to be totally absorbed. The extremely wide variation in time of suture disappearance in the cornea may then be the resultant of many mechanisms, such as varying tissue bites, partial absorption, suture sensitivity, and protein hunger.

Halsted's final objection to catgut, the reaction it excites, does not seem to be a major one here. In rabbit corneas no more pronounced reaction was demonstrated to catgut sutures than to silk. In the patients reported in this series, suture reaction was no major factor in determining success or failure of the surgical procedure. In corneal surgery the advantages of a suture which does not

have to be removed seems to outweigh the disadvantages of any slight increased reaction to absorbable sutures.

Catgut should appeal to the ophthalmologist in closing corneal wounds because it is composed almost entirely of collagen fibers and is therefore the most similar substance to corneal tissue available.

Summary and Conclusions

The history of the development of catgut sutures in general surgery and in anterior segment ocular surgery is reviewed. The composition of modern catgut sutures as standardized by the *U. S. Pharmacopeia* is presented.

Individual catgut sutures were biopsied, cultured in fluid thioglycolate media and found to be sterile.

The reaction of rabbits' corneas to silk, plain catgut and medium chromic catgut sutures was evaluated. In 28 days there was little difference in the reaction excited by these three suture materials in clear corneal incisions. Epithelization of the suture track was found to be as common with catgut sutures as with silk.

Rabbits previously sensitized to an extract of plain or chromic catgut showed little difference in the corneal reaction to these suture materials as compared with rabbits not previously sensitized.

Plain and medium chromic catgut sutures were used in the closure of clear corneal lacerations in 26 patients. There was no instance of postoperative wound separation or poor wound healing. Suture reaction and corneal scarring were not pronounced although subjective ocular irritation was moderate in three patients.

Plain and medium chromic catgut were used in the direct suture of two lamellar and nine penetrating keratoplasties. Wound separation or iris prolapse did not occur, and wound healing was considered satisfactory. Corneal scarring and suture reaction were not pronounced.

The disappearance times of plain and chromic catgut sutures from human corneas were studied and found to vary from five to 38 days for plain catgut and from eight to 64 days for chromic catgut. It is thought that the wide range of disappearance time is due to many factors, including the patient's reaction, the suture material and the surgical technique.

Halsted's objections to the use of catgut sutures are re-evaluated. Most of these no longer seem to apply to modern day catgut.

Catgut is a satisfactory suture material for the closure of clear corneal wounds, and its absorbable quality offers a distinct advantage over silk.

1110 West Main Street.

References

1. Gordon, B. L.: Medicine Throughout Antiquity. Philadelphia, Davis, 1949.
2. Major, R. H.: A History of Medicine. Springfield, Ill., Thomas, 1954.
3. Mettler, C. C.: History of Medicine. Philadelphia, Blakiston, 1947.
4. Encyclopaedia Britannica, Chicago, William Benton, **5**:31, 1956.
5. Graham, H.: The Story of Surgery. New York, Doubleday, 1939.
6. Guthrie, D.: Lord Lister. Edinburgh, E. and S. Livingstone Ltd., 1949.
7. Leonardo, R. A.: History of Surgery. New York, Frober Press, 1943.
8. Localio, S. A., Casale, W., and Hinton, J. W.: Wound healing: Experimental and statistical study; II. Sutures and ligatures. Internat. Abstr. Surg., **77**:457, 1943.
9. Halsted, W. S.: Ligature and suture material. J.A.M.A., **60**:1119 (Apr.) 1913.
10. Marchesani, O.: Ueber catgutanaphylaxie. Ber. Versamml. deutsch. ophth. Gesellsch., **49**:233, 1932.
11. Frugoni, P.: Sulla supposta allergia da catgut. Arch. ital. di diur., **43**:334, 1936.
12. Kraissl, G. J., Kesten, B. M., and Cimiotti, J. G.: Relation of catgut sensitivity to wound healing. Surg. Gynec. & Obst., **66**:628, 1938.
13. Erdmann, J. F.: Recognition and treatment of postoperative complications. South. Surgeon, **2**:193, 1933.
14. Thompson, W. D., Ravdin, I. S., Rhoads, J. E., and Frank, I. L.: Use of lyophile plasma in correction of hypoproteinemia and prevention of wound disruption. Arch. Surg., **36**:509, 1938.
15. Meleney, T. L.: Problem of catgut sterility. Internat. Abstr. Surg., **71**:422, 1940.

16. The Pharmacopeia of the United States of America, Eleventh Decennial Revision. Easton, Mack Printing Co., 1941.
17. Localio, S. A., Casale, W., and Hinton, J. W.: Wound healing—experimental and statistical study: III. Experimental observations. Surg. Gynec. & Obst., **77**:243, 1943.
18. ———: Wound healing—experimental and statistical study: IV. Results. Surg. Gynec. & Obst., **77**:376, 1943.
19. ———: Wound healing—experimental and statistical study: V. Bacteriology and pathology in relation to suture material. Surg. Gynec. & Obst., **77**:481, 1943.
20. Madsen, E. T.: An experimental and clinical evaluation of surgical suture materials. Surg. Gynec. & Obst., **97**:73, 1953.
21. ———: An experimental and clinical evaluation of surgical suture materials: II. Surg. Gynec. & Obst., **97**:439, 1953.
22. ———: An experimental and clinical evaluation of surgical suture materials: III. Surg. Gynec. & Obst., **106**:216, 1958.
23. Hughes, W. L.: Catgut sutures in cataract extractions. Arch. Ophth., **29**:867, 1943.
24. Hughes, W. L., Guy, L. P., and Romaine, H. H.: Absorbable sutures in cataract surgery. Arch. Ophth., **32**:362, 1944.
25. Davis, F. A.: Catgut sutures for closure of the deep corneoscleral wound in operations for cataract; A preliminary report. Arch. Ophth., **31**:321, 1944.
26. Alger, L. J.: Use of absorbable corneoscleral sutures in cataract surgery. Arch. Ophth., **38**:665, 1947.
27. Davis, F. A.: Incision and closure of the wound in cataract operations. Arch. Ophth., **44**:175, 1950.
28. Fralick, F. B.: 6-0 chromatized gut in wound closure after cataract extraction. West Virginia M. J., **46**:251, 1950.
29. Dunnington, J. H., and Regan, E. F.: The effect of sutures and of thrombin upon ocular wound healing. Am. J. Ophth., **35**:167, 1952.
30. ———: Absorbable sutures in cataract surgery. A.M.A. Arch. Ophth., **50**:545, 1953.
31. Taylor, J. W.: Absorbable postplaced sutures in cataract surgery. J. Florida M. J., **7**:479, 1952.
32. Roberts, W.: Buried sutures for closure of cataract incisions. Am. J. Ophth., **35**:1459, 1952.
33. Stocker, F. W.: The use of corneoscleral gut sutures. Am. J. Ophth., **42**:730, 1956.
34. ———: On suturing in cataract surgery. Cincinnati J. Med., **38**:289, 1957.
35. Fralick, F. B.: Wound closure with catgut. Am. J. Ophth., **35**:263, 1952.
36. Kirby, D. B.: Use of direct radial mild chromic-gut sutures in penetrating keratoplasty. Am. J. Ophth., **38**:349, 1954.
37. Paton, R. T., Keratoplasty. New York, McGraw-Hill, 1955.
38. Kronenberg, B.: Recent advances in ocular sutures. Am. J. Ophth., **46**:49, 1958.
39. The Pharmacopeia of the United States of America, Fifteenth Revision, Easton, Mack Publishing Co., 1955.
40. Martin, E. W., and Cooke, E. F.: Remington's Practice of Pharmacy. Easton, Mack Publishing Co., 1956.
41. Ethicon Suture Handbook. Somerville, New Jersey, Ethicon Inc., 1954.
42. Narat, J. K., Congelosi, J. P., and Belmonte, J. V.: Electron sterilization of catgut. Surgery, **41**: 324, 1957.
43. Germuth, F. G., Jr., Maumenee, A. E., Pratt-Johnson, J., Senterfit, L. B., Van Arnam, C. E., and Pollack, A. D.: Observations on the site and mechanisms of antigen-antibody interaction in anaphylactic hypersensitivity. Am. J. Ophth., **46**:283 (Nov. Pt. II) 1958.
44. Van Winkle, Walton, Jr., Sewell, W., and Wiland, J.: Mechanism of absorption and antigenicity of absorbable collagen sutures. J. Am. Geriat. Soc., **3**:572, 1958.
45. Snell, A. C., Jr.: Perforating ocular injuries. Am. J. Ophth., **28**:263, 1945.
46. Duke, J. R., and Schimek, R. A.: Perforating injuries of the globe. Am. J. Ophth., **36**:375, 1953.

VON HIPPEL-LINDAU DISEASE

MAXWELL THOMAS, M.D., AND RONALD M. BURNSIDE, M.D.
Dallas, Texas

This report presents a family with multiple hemangiomatosis, von Hippel-Lindau disease, involving the eyes, central nervous system, and kidneys with about equal frequency. The family consists of five generations (fig. 1). There are three generations with this uncommon, dominate type, hereditary disease under observation at the present

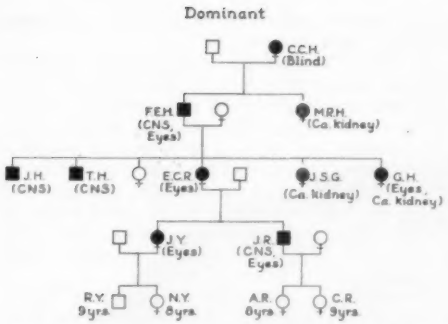


Fig. 1 (Thomas and Burnside). Von Hippel-Lindau disease, affecting 10 patients in four generations.

time. This disease may have some neoplastic characteristics, it may be malignant in vital organs, and it may actually become malignant by change.

The subject of angiomatosis retinae has been reviewed in a number of ways. The last and most complete review on the subject was by Vail, who reported a case that was treated with diathermy and, 11 years later, again reported this case. The syndrome of von Hippel-Lindau disease has become an established entity. Ida Mann and Sorsby have stated that it would seem to be a dominant form of disease but the genetic behavior cannot be completely established, due to the insufficient number of case histories available. Most of the literature on the subject has been in the form of case reports and treatments.

Bird and Krynauw presented one of the most complete reports of Lindau disease in a South African family. These authors felt that this disease was not sex-linked. MacDonald reported two generations in two different families. There were six cases of the disease in 11 members of these families. These two reports are among the more complete in recent literature but no definite conclusions could be drawn from them.

Considering the heredity and development of this disease, one wonders what takes place in the blood vessels to allow the typical round tumor mass to form. It could be a pathologic process in the retinal vessels themselves, similar to the telangiectasis retinae described by Reese who states that the advanced stages of the two diseases may resemble each other, although the age groups are characteristically different. Reese does suggest, however, that the pathologic changes which obstruct the vessels cause dilation and resulting nutritional defects. In a recent article, Vail says that the ages of the patients range from three to 60 years, with an average of 25 years. In the present case reports none of the patients were in the lower age groups.

Case histories

C. C. H., the mother of the following generations and apparently the first reported source of the disease, died of cancer of the kidney.

F. E. H., the first daughter of C. C. H., and the mother of the following generations, lost the sight of her right eye between the age of 17 and 18 years. She gradually became more helpless and died at the age of 48 years.

M. R. H., the spinster daughter of C. C. H., lost the sight in both eyes before she finished high school. Her family thought at this time that her loss of sight was due to malaria fever and studying too hard. She died at about the age of 32 years of unknown causes.

T. H., son of F. E. H., died of brain tumor in 1951. Diagnosis, Lindau disease, Baylor University Hospital, Dallas, Texas.

G. H. was first seen by an internist on August 24, 1949, for a physical check-up. No serious complaint and no disease was found. The eyes were not examined at this time. On January 21, 1950, the patient came in for an eye examination with the complaint of black spots in the vision of the right eye since November 28, 1949. It was stated that this was sudden in onset. Vision was: R.E., counting fingers; L.E., 20/20. Fundus examination of right eye showed a large area of central chorioretinitis with a single sacculation and aneurysm of the inferior temporal arteriole. There was a four-degree central scotoma. The patient developed a temporal detachment of the retina on September 1, 1951, and was started on contact X-ray therapy with the Philips unit on September 11, 1951, to a total of 6,000 r. The detachment flattened and the vascular lesion became less active. On April 22, 1953, the urologist diagnosed a hypernephroma of the right kidney which was confirmed by surgery. The patient died on September 29, 1953, from extensive metastasis.

E. C. R. was first seen August 11, 1942, by an internist when she was 35 years of age. Her chief complaint was black spots in the temporal field of the right eye. Eye examination at this time indi-

Fig. 2 (Thomas and Burnside). E. C. R. Photomicrograph of section from right eye, showing tumor mass in retina.

cated von Hippel disease, with vision in the left eye being 20/20. Examination on December 8, 1942, showed a patch of old choroiditis in the right eye just above the macula. There was a V-shaped peripheral area in the lower portion of the eye in which there was no retina or choroid. There were two large dilated vessels which appeared to anastomose in this area. Diagnosis: absolute glaucoma, right eye, due to von Hippel disease. On February 17, 1954, this patient was operated upon. Enucleation of the right eye was done at this time.

Pathologic reports and gross description (fig. 2). RIGHT EYE. The retina was detached. Protein-rich coagulum filled the vitreous and subretinal spaces. The chamber angle was completely obliterated by a wide peripheral anterior synechia. There was a thin fibrovascular membrane lining the anterior surface of the iris which was atrophic and fibrotic. The lens was posteriorly subluxated with metaplastic fibrosis of the anterior subcapsular epithelium. The ciliary body showed atrophy and fibrosis of its processes. A markedly disorganized retina was detached with subretinal protein-rich coagulum.

In one area of the peripheral retina a mass was noted, consisting chiefly of capillary spaces surrounded by focal glial proliferation. Among the vessels were characteristic swollen pseudoxanthomatous cells containing foamy cytoplasm. Occasional thick-walled vessels and foci of fibrosis circumscribed by pigment were noted in Van Gieson-stained sections. Some of the capillary spaces contained blood.

Hyperplasia of pigmented and nonpigmented epithelium of the adjacent pars plana of the ciliary body was observed. The underlying choroid showed a large area of fibrosis and pigmentation. Fibrovascular tissue adhered to the surface of the tumor mass and extended across the vitreous connecting to the opposite detached retina. On the side of the tumor, near the optic disc, several markedly dilated retinal vessels were noted. Retinal cysts containing coagulum were seen.

In some of the sections studied near the posterior pole the choroid showed focal fibrosis, ossification, and lymphocytic infiltration. There were no definite changes of the sclera. The optic disc showed a deep glaucomatous cup. A focus of foam cells was seen on one area of the base of the optic cup. A band of glial tissue arose from the optic disc and extended across the cup to connect to the detached retina. A considerable increase of the fibrous and glial tissue of the optic nerve was present, indicating optic atrophy.

Diagnosis. (1) Angiomatosis retina (von Hippel disease), (2) retinal detachment with retinal cyst, (3) secondary glaucoma, (4) subluxation of the lens, (5) anterior complicated cataract, (6) ectropion uvea, (7) optic nerve atrophy.

J. E. R.—This patient was first seen on April 23, 1951, with the following findings: Vision 20/20 both eyes. Both eyes normal to external examination; muscle balance was normal; pupillary reactions were normal. Fundus of the right eye showed a clear media; the right optic disc margin was well outlined, with no edema present. The superior retinal arteries showed a single sacculation while still on the disc. One or two disc diameters off of the disc this arteriole presented multiple sacculations—in formation like a string of beads. The aneurysm was seen at the equator at approximately the 3:30-o'clock position, showing a large sacculation with exudation and possibly flat detachment of the retina. The associated veins were dilated and more irregular than normal. No definite lesion could be visualized in the left fundus. Visual fields, peripherally and centrally, both white and colored, were normal except for a large scotoma in the inferior nasal field, right eye. Impression: von Hippel disease.

The patient was next seen on October 23, 1953. One year prior to this time the patient had developed neurologic lesions in the spinal cord, which were treated with X-rays with good response. There was a typical round, tumorlike lesion of the right eye still present. This had been treated by X-rays at repeated intervals as follows:

May 12, 1951, Phillips X-ray 40 by 60 by 10 N. F. medial portion right eye. May 19, 1951, Phillips X-ray 40 by 30 by 10 N. F. medial portion right eye. May 30, 1951, Phillips X-ray 40 by 30 by 10 N. F. medial portion right eye. September 29, 1951, radiotherapy completed.

Examination on October 23, 1953, showed the development of a typical aneurysm with new exudates and vessel changes of 90 degrees in the left eye.

Operation on March 29, 1954, consisted of cauterization with the Walker equipment of the arteriovenous aneurysm. A detachment procedure was done on the right eye. On May 4, 1954, cauterization with the Walker equipment of the arteriovenous aneurysm was repeated. A detachment procedure was done on the left eye.

The X-ray treatment was repeated on the right

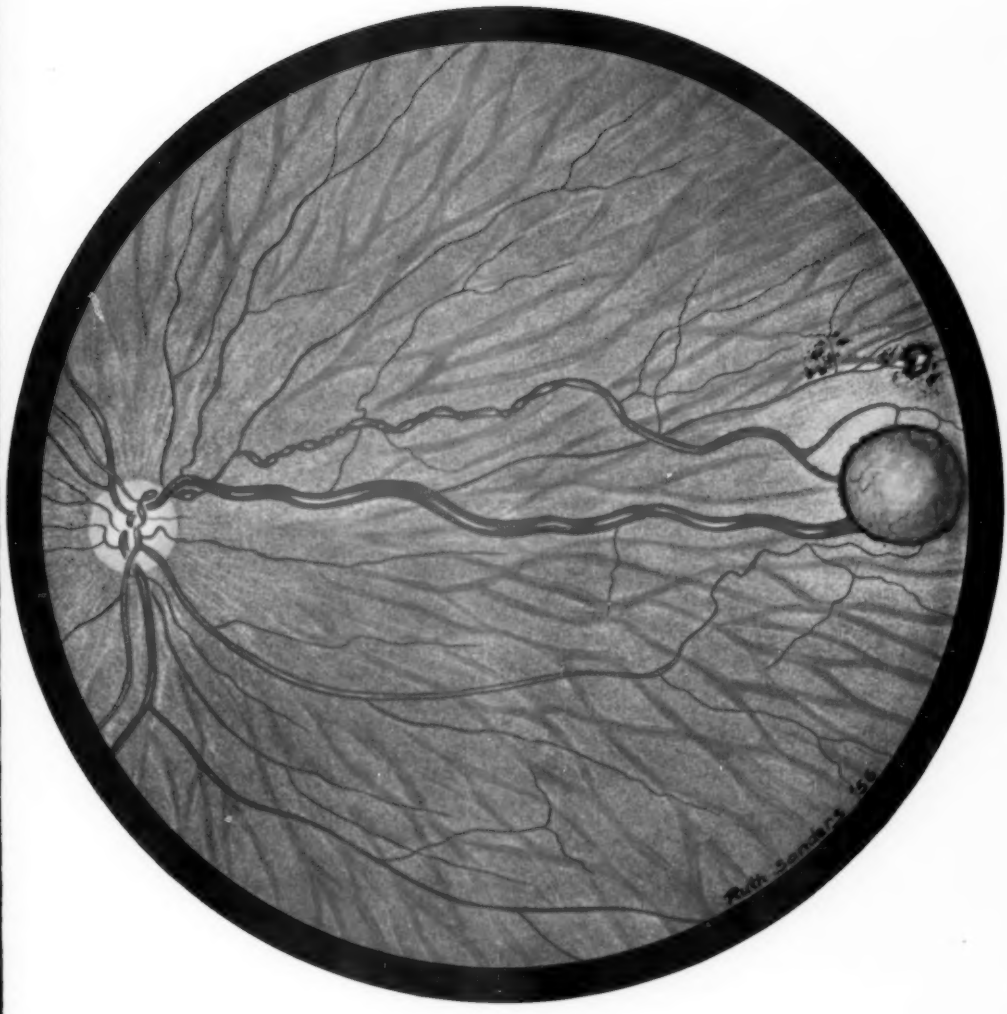


Fig. 3 (Thomas and Burnside). Retinal angioma of the right eye.

eye: January 7, 1955, 40 by 30 by 10 = 1,250 r medial portion; November 11, 1955, 40 by 30 by 10 = 1,250 r (45 sec., distance about 43 mm.); November 21, 1955, 40 by 30 by 10 = 1,250 r (45 sec. distance about 43 mm.). A consultant examination on March 9, 1956, showed the usual dilation in the right eye; in some areas there was almost sausage appearance of the blood vessels. The aneurysm, resembling a toadstool, was about at the 3-o'clock position in right eye. It had a pinkish color and protruded into the vitreous. This lesion seemed to be free but was attached somewhere behind the areas the diathermy treatment already described had been done. No area of diathermy was seen, particularly below. In the right eye the aneurysm was on the nasal side. Since hemorrhages are frequent with treatments by such known methods as diathermy, electrolysis, and radiation it seemed best to leave well enough alone at this time.

In the macula of the left eye, there was a whitish mass, dilated vessels, and an area extending up toward the 1-o'clock and to the 3-o'clock positions. It was also noted that a large group of vessels branched out above. The retinal vessels covered over the mass. Some evidence of crystalline material was seen in the fundus. Evidence of the previous diathermy treatment could be seen. There was a question as to whether an exudative type of lesion might occur if the right eye were treated further.

Comment

Our observations suggest that several findings might be added to this disease. Persons so afflicted seem to develop eye signs during their late twenties or early thirties. The lesions begin as a small sacculation on an arteriole in the retina or as an explosive chorioretinitis, which may be destructive as far as vision is concerned. As in two cases, the lesions may regress in the fourth decade, possibly due to early sclerosis of the defective vessel walls.

Five of the presently living patients have for the past three years been under continuous treatment with CVP or Duo-CVP, a combination of water-soluble bioflavonoid complex with ascorbic acid, with dosages of six and three capsules daily, respectively. During this period no increase in activity of their lesions has been observed. The rationale for the use of CVP is based on extensive experimental and clinical studies indicating that the water-soluble bioflavonoids derived from the citrus fruits are of value in restoring and maintaining the integrity of the smaller blood vessels and that this action is enhanced by ascorbic acid. It has also been reported that the bioflavonoids possess an anti-inflammatory action.

Therapeutic measures tried in the past, fever therapy, Percortin, radiation, and local diathermy, have not proved satisfactory. X-ray therapy does seem to reduce the size of the lesions and improve vision. It also seems to improve the central nervous system lesions. Diathermy cauterization of the lesions was only temporarily effective, with new growth recurring around or through areas of scarring. The newer steroids and CVP appear to be of definite value in acute episodes, in prevention of hemorrhages, and offer some hope for retarding or arresting completely the progress of the disease.

Four members of the younger generation, aged six to eight years, seem to have no signs of disease. This seems to indicate that von Hippel disease is not congenital in origin, that is, present at birth. Two individuals apparently have recovered, or their lesions have regressed, at 35 to 40 years of age. The patient, J. E. R., with a solitary, markedly elevated aneurysm in the right eye might be benefitted by actinic cauterization as recommended by Prof. Meyer-Schwickerath.

It becomes increasingly difficult to discuss any disease that assumes so many forms and is found in so many organs besides the eye.

Ryan reported a case that was probably due to a congenital abnormality of the retinal vessels. After a period of time, there were no associated disturbances in the child; however, one must not expect this to be typical of the disease.

It should be noted that following diathermy treatment, the vision of one eye was entirely lost. This therapy seemed to precipitate massive choroiditis, similar to that which follows if the lesion is allowed to continue without treatment. The one remaining eye of the patient, J.E.R., is shown in Figure 3. The retina seems to be in place following

diathermy, but the little tumor itself has not been destroyed. There is, however, some hesitancy in repeating the diathermy because of the difficulty in pinpointing the lesion and danger of disturbing the vitreous. Although the Meyer-Schwickerath technique would seem to be the method of choice, needed equipment is not available.

In a family, such as the one here reported, one should be constantly on the alert for pathologic changes in organs other than the eye. Observation of this family should be continued over the years. The ophthalmologist should view with suspicion any definite changes seen in the eyes. It is not certain that these diseases progress to destroy the eye, as there is some evidence of regression, perhaps due to sclerotic changes that take place in the vessels of the aging. If this is an hereditary disease, perhaps in the future it will be learned that something in the metabolism or nutritional status of these patients cause this disease of the blood vessels.

4105 Live Oak Street (21).

ACKNOWLEDGMENT

We wish to thank the Medical Arts Department, Southwestern Medical School, University of Texas, for the drawing and the U. S. Vitamin Corporation for CVP.

REFERENCES

Mann, I.: Developmental Abnormalities of the Eye. Cambridge, 1937, p. 142.

Sorsby, A.: Genetics in Ophthalmology. St. Louis, Mosby, 1951, p. 239.

Bird, A. V., and Krynouw, R. A.: Lindau's disease in a South African family. Brit. J. Surg., **40**:443-437 (Mar.) 1953.

MacDonald, A. E.: Lindau's disease, Arch. Ophth., **23**:564-576 (Mar.) 1940.

Reese, A. B.: Telangiectasis retinae. Am. J. Ophth., **42**:1-8 (July) 1956.

Vail, D.: Angiomatosis retinae; Eleven years after diathermy coagulation. Am. J. Ophth., **46**:525-534 (Oct.) 1958.

Ryan, E. P.: Angiomatosis retinae: Clinical note. Arch. Ophth., **23**:623 (Mar.) 1940.

OPHTHALMIC MINIATURE

"I confess, however, that I am unable to understand how you arrive at the double visit to the optician."

Holmes took the glasses into his hand.

"You will perceive," he said "that the clips are lined with tiny bands of cork to soften the pressure upon the nose. One of these is discolored and worn to some extent, but the other is new. Evidently one has fallen off and been replaced. I should judge that the older of them has not been there more than a few months. They exactly correspond, so I gather that the lady went back to the same establishment for the second."

Sir Arthur Conan Doyle,
The Adventure of the Golden Pince-Nez.

NOTES, CASES, INSTRUMENTS

ALPHA CHYMOTRYPSIN IN INTRAOCULAR FOREIGN BODY EXTRACTION

HENRY L. HILGARTNER, M.D.
AND
HARDY E. THOMPSON, JR., M.D.
Austin, Texas

Following is a report of the successful use of alpha chymotrypsin to remove a traumatic cataract followed by extraction of a metallic foreign body from the vitreous through the pupil.

CASE REPORT

On November 30, 1959, Mr. E. A. K., aged 47 years, was struck in the left eye by a piece of metal while hammering on a nail. He was first seen on December 1, 1959.

Examination. O.S. The cornea showed a linear penetrating wound midway between the center of the cornea and the limbus at the 9-o'clock position. The iris was torn, and the lens showed a large area of clouding nasally. The rest of the lens was clear. The foreign body could not be seen.

X-ray report (Dr. Emmett Doles). Films of the orbits show a 1.0 by 1.0 by 1.5 mm. opaque foreign body within the left eye with a localization chart.

The foreign body was located 15 mm. behind the center of the cornea, 4.0 mm. above the horizontal plane of the cornea, and 0.0 mm. nasal side of vertical plane and 0.0 mm. temporal side of vertical plane of the cornea.

Operation. An intracapsular cataract extraction was done on the left eye and a metallic foreign body was removed with a magnet on December 7. Akinesia was according to the Van Lint method with one-percent Procaine and one cc. of one-percent Procaine was injected retrobulbarly. Cocaine (five and 10 percent) was applied topically. The bulbar conjunctiva was incised at the limbus at the 12-o'clock position and the incision was carried down to the 9- and 3-o'clock positions, respectively, and the conjunctiva was dissected back two to three mm. Sutures (6-0 black silk) were placed in the cornea at the limbus at the 10:30 11:30, 12:30 and 1:30-o'clock position. The point of a keratome was passed through the limbus at the 12-o'clock position into the anterior chamber. The incision was enlarged with Castroviejo scissors to the 9-o'clock position and the sutures were placed in the scleral lip adjacent to the corneal insertion. The incision was then enlarged on the temporal side to the 3-o'colck position and the sutures were placed similarly in the sclera. The iris was grasped, withdrawn and excised with DeWecker scissors at the 11-o'clock position.

Alpha chymotrypsin (Zolyse) was then introduced into the posterior chamber. After four minutes, the lens became more convex and shifted forward slightly. The lens was removed with an erisophake en capsule, without loss of vitreous. The magnet was then introduced into the anterior chamber and the current was turned on. It required several attempts before the foreign body was attracted and attached to the magnet and removed. At no time was any vitreous lost. The sutures were then tied, the pillars replaced, and an air bubble was injected into the anterior chamber.

The postoperative course was uneventful and the patient was discharged from the hospital after one week. The eye healed with no complications.

On February 22, 1960, the patient reported for observation. With a +10D. sph. $\bigcirc$ +1.5D. cyl. ax. 30° in the trial frame, the vision was 20/24—2.

Pathologic report. Intraocular foreign body, left eye.

Gross. Submitted is the lens of the left eye which is yellowish, opaque, and measures 1.8 mm. in diameter. The lens is covered by a friable, grayish-white capsule. This specimen is not submitted for microscopic examination.

Diagnosis. Traumatic cataract, foreign body, left eye.

Follow-up. On March 21, 1960, the patient was fitted with a contact lens, giving him a vision of 20/24. On July 1, 1960, to improve the vision in the normal eye, ordinary lenses were prescribed, to be worn with the contact lens in position on the left cornea. The prescription was: R.E., +0.5D. sph. $\bigcirc$ +0.25D. cyl. ax. 90° = 20/16; L.E., +0.5D. sph. = 20/20; Add: R.E., +2.75D. sph. $\bigcirc$ +0.25D. cyl. ax. 90° = J1 at 16 inches; L.E., +2.5D. sph. = J2 at 16 inches.

COMMENT

The extraction of the traumatic cataract was considered intracapsular, although there was a small tear in the lens capsule anteriorly and posteriorly where the foreign body had penetrated. The fact that these tears did not enlarge or leak any lens cortex can be accounted for only by the zonulolysis of the alpha chymotrypsin; the lens was completely free and no traction had to be applied to the zonules.

As the foreign body was about 15 mm. behind the lens, we know the hyaloid face was ruptured as the lens was penetrated and as the foreign body was extracted by the mag-

net. However, on examination with the slitlamp, the vitreous face is now intact and flat, and well behind the margins of the iris. No evidence of the damage to the vitreous by the foreign body or the alpha chymotrypsin can be seen at this time.

Summary

A case of an intraocular foreign body is reported in which the cornea, iris, lens, and vitreous were penetrated and the metallic object was lodged in the vitreous chamber. By using alpha chymotrypsin, extraction of the traumatic cataract was accomplished with an erisophake en capsule without loss of vitreous. The foreign body was removed through the cataract incision, thereby leaving the sclera, choroid, and the retina intact. The patient experienced one operative procedure and one hospitalization instead of two.

202 West 13th Street.

POSTERIOR EMBRYOTOXON*

Report of an interesting case

Frederick C. Wuest, Lieut. (MC), USN,
and
Wayne L. Erdbrink, Comdr. (MC), USN
Oakland, California

Posterior embryotoxon (Axenfeld[1]), congenital hyaline membrane of the anterior chamber (Mann[2]), or the prominent anterior border ring of Schwalbe (Burian, Braley, and Allen[3]), has an interesting and unusual appearance on slitlamp and gonioscopic examination. Hypoplasia of the anterior stromal layer of the iris, corectopia and polycoria may be found concomitantly. Glaucoma also is found occasionally, but probably is not causally related.[3]

Axenfeld[1] was the first to describe a white annular band on Descemet's membrane at the peripheral cornea with adherent iris strands. This he called a posterior embryotoxon, and suggested that the whole formation might possibly be a rudimentary pectinate ligament in man. Ida Mann[2] mentioned the possibility of fetal inflammation as a cause of the membrane. However, an embryologic explanation was more likely. The postendothelial tissue, which forms the anlage of the pupillary membrane and anterior layer of the iris stroma, may remain too long in contact with the periphery of the cornea and might lead to the formation of the hyaline tissue there.

Burian and coworkers[3] were of the opinion that this "hyaline membrane" is an extended thinned trabecula and the prominent ring is that of Schwalbe. They[4,5] stated that this prominent ring of Schwalbe and pectinate ligament features should not be thought of as "mesodermal remnants" resulting from failure of atrophy and resorption of normal mesodermal tissue, but are the result of excessive laying down of mesodermal tissue in embryonic and fetal eyes. Their comparative anatomic studies show that analogies to all forms of pectinate fiber anomalies occurring in man are found in the normal chamber angles of animals, and represent in man genetically determined atavistic traits. In microscopic examination of 600 eyes, they found that 15 percent showed a prominent anterior border-ring. This incidence very nearly approached their clinical impression of its occurrence.

Case report

D. G. C., a 24-year-old white seaman, was examined in December, 1959, for a refraction. The only complaint was referable to vision and this was corrected by myopic lenses to 20/20 in each eye. The pupils, Schiøtz tensions, motility, and ophthalmoscopy were normal.

External examination of the right eye revealed a white annular band on the posterior cornea extending irregularly about one mm. inside the limbus, being absent only in part of the temporal quadrants. Slitlamp examination showed an increased density of Descemet's membrane; its central border was thickened, somewhat pigmented, and protruded into the anterior chamber. In the inferonasal quadrant, a large iris adhesion was present with the

---

* From the Ophthalmology Branch, EENT Service, U. S. Naval Hospital. The opinions or assertions expressed herein are those of the writer and are not to be construed as official or as necessarily reflecting the views of the Medical Department of the Navy or of the Naval Service at large.

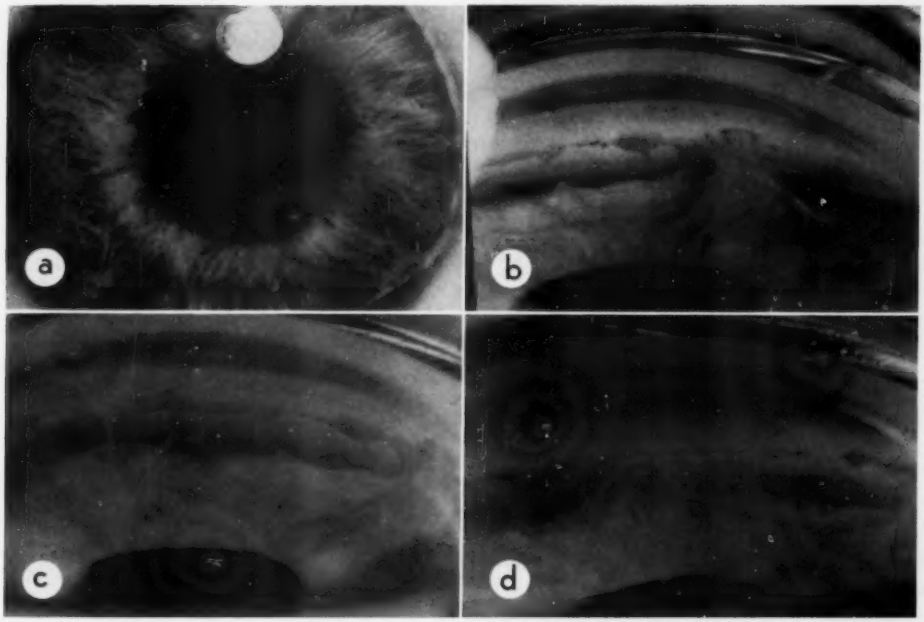


Fig. 1 (Wuest and Erdbrink). D. G. C. Right eye. (a) Nasal embryotoxon and large iris adhesion inferonasally. (b) Gonioscopic view of the inferonasal angle with the large iris adhesion, and (c) of the nasal angle with pectinatelike ligaments. Left eye. (d) Gonioscopic view of the inferonasal angle with bridging iris processes.

peripheral one third of the iris stroma attached to the cornea, anterior to the white annular ring. Beneath this adhesion, the dilator muscle was completely exposed (fig. 1a). Gonioscopic examination revealed the large iris adhesion and smaller bridging iris processes partially obscuring the angle (fig. 1b). In other areas, pectinatelike ligaments could be seen extending from the iris root to Schwalbe's line (fig. 1c).

Gonioscopic examination of the left eye revealed similar bridging iris processes (fig. 1d). No large iris adhesion was visualized, such as was present in the right eye.

Summary

The case of "posterior embryotoxon" here reported appears to be a marked example of an anomalous trabecular zone and a prominent anterior border ring of Schwalbe. From the excellent clinical and microscopic studies of Burian, Braley, and Allen,[3] it is our opinion that their descriptive and embryologic explanations of this anomaly are to be preferred to those of others. Also, using their suggestion, this entity might be properly referred to as an anomalous trabecular zone and a prominent anterior border ring of Schwalbe.

U. S. Naval Hospital (14).

Acknowledgment

We wish to thank Miss Diane S. Beeston, Ophthalmology Clinic, University of California Medical Center, San Francisco, for the gonioscopic photographs used in this case report.

References

1. Axenfeld, T.: Embryotoxon corneae posterius. Ber. d. deutsch. ophth. Gesellsch., Heidelberg, 1920, pp. 301-302.

2. Mann, I.: Developmental Abnormalities of the Eye. Philadelphia, Lippincott, 1957, pp. 277-287, 350.

3. Burian, H. M., Braley, A. E., and Allen, L.: External and gonioscopic visability of the ring of Schwalbe and the trabecular zone: An interpretation of the posterior corneal embryotoxon and the so-called congenital hyaline membranes of the posterior corneal surface. Tr. Am. Ophth. Soc., **52**:389-428, 1954.

4. Allen, L., Burian, H. M., and Braley, A. E.: A new concept of the development of the anterior chamber: Its relationship to developmental glaucoma and other structural anomalies. Arch. Ophth., **53**: 783-789, 1955.

5. ———: The anterior border ring of Schwalbe and the pectinate ligament: Embryologic and comparative anatomic studies. Arch. Ophth., **53**:799-806, 1955.

SCLERAL RIGIDITY DETERMINATIONS

Before and after tonography

J. William Rogers, M.D., and Winston Roberts, M. D.
Winston-Salem, North Carolina

The degree of indentation measured in reading the Schiøtz tonometer depends not only upon the pressure that exists within the eye before the tonometer is applied to the eye, but also upon the degree of resistance that the coats of the eye plus its surrounding tissues exhibit to the deforming force of the tonometer weight.[1] The relationship between the change in pressure and the change in volume of an eye is indicated by a proportionality constant known as the "coefficient of scleral rigidity" or E. The coefficient of scleral rigidity may be represented by the formula:[1]

$$E = \frac{1}{{}^{\Delta}V_e} \log \frac{P_1}{P_2}$$

E = coefficient of scleral rigidity
${}^{\Delta}V_e$ = change in volume of the eye
P_1 = initial intraocular pressure
P_2 = final intraocular pressure

The tables of intraocular pressure for the indentation tonometer, as well as the procedure of tonography, are based in part on the concept of an average scleral rigidity of 0.0215, constant in each eye under all circumstances of intraocular pressure.[2] The average value of 0.0215 for the coefficient of scleral rigidity was derived from paired readings with 5.5 and 10.0 gm. weights made on 500 normal eyes with a Schiøtz tonometer and was used in the tonometer calibration formulas resulting in the tonometer scales of 1948.

Further investigation of the coefficient of scleral rigidity of the living eye, and also studies such as those of Grant and Trotter,[3] using enucleated eyes, revealed similar average values; hence this constant was left unchanged in the derivation of the 1954 scale.

Ballintine[4] found E shifted toward the region of greater rigidity in a series of 479 patients; however, these patients were all glaucoma suspects and the elevated tension in some of these individuals might have been due to elevated scleral rigidity.

It has become apparent that the scleral rigidity is not a constant but varies with a number of both intraocular and extraocular conditions. Scleral rigidity has been noted to be low with myopia, thyrotropic exophthalmos, miotic therapy, and water provocative tests.[5] MacDonald,[6] investigating living human eyes, found an inverse relationship between tension and scleral rigidity, while McBain[7] and Gloster and Perkins[8] found the same relationship using enucleated human eyes.

Errors resulting from the failure to correct results in the individual eye for its scleral rigidity are greatly accentuated in tonography, and attempts have been made to eliminate the necessity of assuming an average value for scleral rigidity. Moses[9] described a method for constant pressure tonography, but felt "the additional equipment and extra operator required for the performance of constant pressure tonography do not at present seem justified by the questionable refinement of results."

Moses and Becker[10] presented two methods of applying a correction for deviations from average values for scleral rigidity, using the Friendenwald 1955 tables and pressure rigidity nomogram plus paired Schiøtz readings or an applanation reading and a single Schiøtz reading. Large differences in the coefficient of scleral rigidity can be found with small changes in Schiøtz scale readings,[1]

TABLE 1

STATISTICAL ANALYSIS OF COEFFICIENT OF SCLERAL RIGIDITY DETERMINATIONS BEFORE AND AFTER TONOGRAPHY

	Coefficient of Scleral Rigidity		Mean Difference	Standard Deviation	Standard Error of Mean	t	Probability
	Paired Schiøtz Before Tonography	Paired Schiøtz After Tonography					
First eye (50 eyes)	0.0226	0.0233	0.00066	0.008	0.0011	0.6	>0.1
Second eye (50 eyes)	0.0216	0.0242	0.00260	0.011	0.0015	1.7	<0.1>0.05
Total (100 eyes)	0.0221	0.0238	0.00163	0.0097	0.00097	1.7	<0.1>0.05

hence the routine application of the methods is not indicated. Rather, paired readings should be repeated and deviation from the average considered significant only if there is a consistent trend toward increased or decreased scleral rigidity.[11]

The present study was undertaken in an effort to ascertain whether there is a significant change of scleral rigidity as a result of tonography and, if present, whether there is a greater change in the second eye tested. The coefficients of scleral rigidity were determined by the application of paired Schiøtz readings to the Friedenwald 1955 nomogram, using scale readings obtained with 5.5 and 10.0 gm. weights, except in the case of four tonograms where 7.5 and 10.0 gm. weights were used because of elevated pressure.

Fifty patients and 100 tonograms are represented, all of which were carried out on patients with glaucoma or on glaucoma suspects. The age range for the group was 24 to 77 years. The initial readings were taken on both eyes, with the patient in the recumbent position, immediately before the start of tonography and the final readings 1.5 to 2.0 minutes following the completion of tonography on each eye. On 35 patients, applanation tonometry was also carried out prior to tonography and the coefficient of scleral rigidity determined using this value and a single reading obtained with the Schiøtz tonometer. Statistical analysis of the data is shown in Table 1.

The differences noted in E before and after tonography cannot be considered significant, the probability being $0.1 > 0.05$ that it might have occurred by chance alone. The same conclusion was also reached by Stepanik[12] following a similar survey of 100 eyes, part normal and part glaucomatous eyes. The average coefficient of scleral rigidity, obtained using the Goldmann applanation tonometer combined with the Schiøtz tonometer, was noted to be 0.0210 which closely corresponds to the accepted value of 0.0215.

SUMMARY

Based on the present study, it is concluded that there is no significant change in scleral rigidity as a result of tonography.

Department of Ophthalmology,
Bowman Gray School of Medicine.

REFERENCES

1. Friedenwald, J. S.: Contribution to the theory and practice of tonometry. Am. J. Ophth., **20**:985-1024 (Oct.) 1937.
2. Goodside, V.: Ocular rigidity: Clinical study. AMA Arch. Ophth., **62**:839-841 (Nov.) 1959.
3. Grant, W. M., and Trotter, R. R.: Tonographic measurements in enucleated eyes. AMA Arch. Ophth., **53**:191-200 (Feb.) 1955.
4. Ballintine, E. J.: Tonography and aqueous humor dynamics: The effect of variation in scleral rigidity on the apparent facility of aqueous drainage as calculated from tonographic measurements. Acta XVII Conc. Ophth., 1954, **3**:1516-1531, 1955.
5. Becker, B., and Gay, A. J.: Applanation tonometry in the diagnosis and treatment of glaucoma: An evaluation of decreased scleral rigidity. AMA Arch. Ophth., **62**:211-215 (July) 1959.

6. MacDonald, R. K.: Symposium on the clinical assessment of glaucoma with particular reference to diurnal variations in pressure: Observations and interpretations. Tr. Canadian Ophth. Soc., **7**:178-184, 1955.

7. McBain, E. H.: Tonometer calibration: II. Ocular rigidity. AMA Arch. Ophth., **60**:1080-1091 (Dec.) 1958.

8. Gloster, J., and Perkins, E. S.: Distensibility of human eye. Brit. J. Ophth., **43**:97-101 (Feb.) 1959.

9. Moses, R. A.: Constant pressure tonography. AMA Arch. Ophth., **59**:527-531 (Apr.) 1958.

10. Moses, R. A., and Becker, B.: Clinical tonography: The scleral rigidity correction. Am. J. Ophth., **45**:196-208 (Feb.) 1958.

11. Schneider, J., Feldstein, M., and Kornzweig, A. L.: Scleral rigidity and tonometry in the aged. Am. J. Ophth., **48**:643-647 (Nov.) 1959.

12. Stepanik, J.: Wird die Skleralrigidität durch die Tonographie beeinflusst? Klin. Monatsbl. f. Augenh., **130**:585-587, 1957.

BILATERAL NUCLEAR OPHTHALMOPLEGIA*

Report of a case with cerebellar symptomatology

R. Douglas Collins, M.D.
Philadelphia, Pennsylvania

Reports in the American literature of cases of bilateral nuclear and supranuclear oculomotor ophthalmoplegia of the Parinaud variety are rare, only three cases having been reported in 20 years. For this reason, the following case with associated cerebellar symptomatology and unusual recovery is being reported.

Case report

A 69-year-old white woman entered the Harrisburg Polyclinic Hospital for the third time on August 8, 1959, with the chief complaint of sudden onset of blurred vision and staggering gait. She had had two previous admissions for an appendectomy in 1930 and lysis of adhesions one year later. One year prior to the present admission she had come under treatment for shortness of breath, ankle edema, and high blood pressure (200/?) with digitalis and Raudixin. Aside from a one-hour headache three weeks prior to admission, she had been in her usual state of health until 24 hours before entering the hospital when she suddenly developed blurred vision and staggering gait to the left, while walking from her kitchen to the bathroom. These symptoms were constant up to admission.

Examination showed a medium built, moderately nourished, elderly woman, who looked her age. The physical findings were limited to the vascular and nervous systems. There was total irregularity of cardiac rate and intensity of sounds with a Grade III apical protosystolic murmur transmitted over the entire precordium. Blood pressure was 180/110.

There was Grade II arteriosclerotic retinopathy. The right pupil was mydriatic and did not react to light, accommodation, and consensual stimulation. There was paralysis of direct upward gaze bilaterally, paralysis of downward gaze on the right, and paralysis of convergence. There was no paralysis of lid retraction. Cerebellar signs were a body curvature to the left, Romberg to the left regardless of whether eyes were open or closed, wide-base ataxia, dysdiadochokinesia of left hand, dysmetria, with a mild tension tremor.

Laboratory findings were quantitative Kolmer of 8.0 units; urine—1 + albumin, PSP—40 percent dye excretion in one hour; BUN—20.2 mg. percent; spinal fluid protein—56 mg. percent Wassermann—weakly reactive; colloidal gold—000111000. EKG showed auricular fibrillation and L.B.B.B. Skull X-ray films, small calcifications above sella turcica.

The course is described by the diagram in Table 1.

Discussion

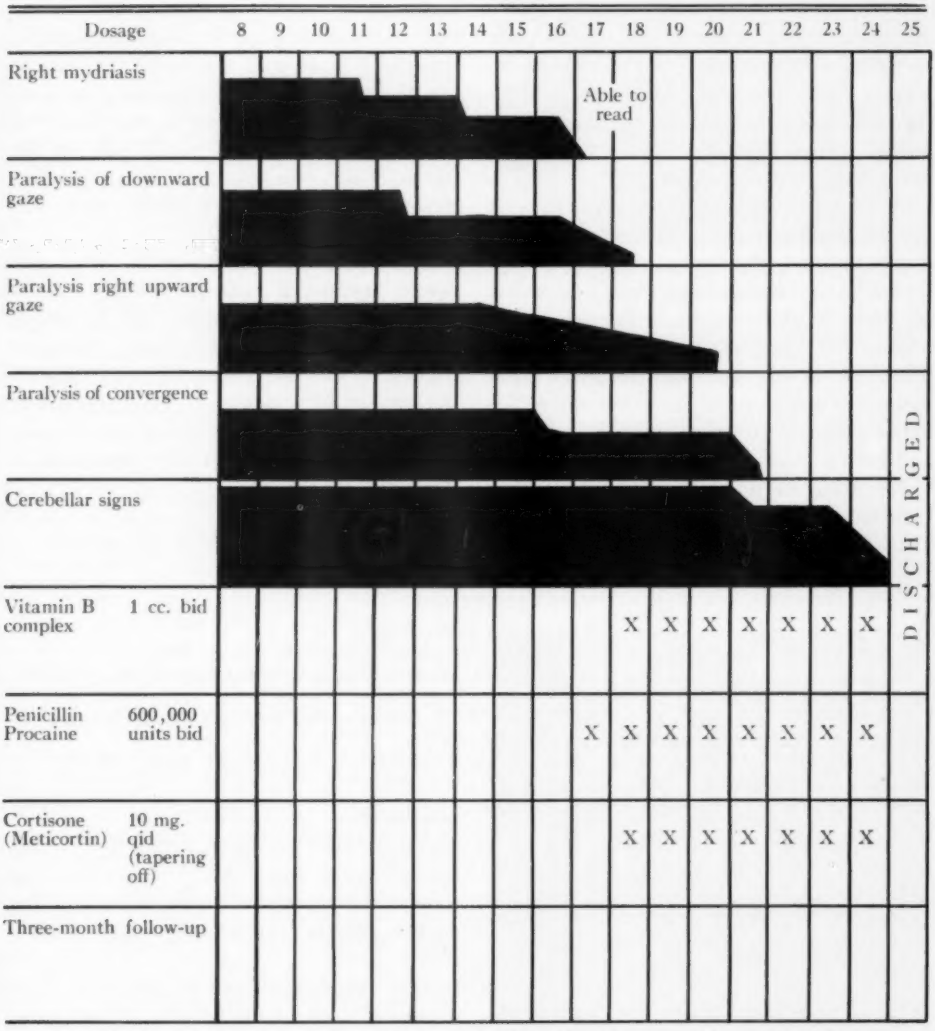
This patient showed bilateral nuclear ophthalmoplegia of the Parinaud variety with the additional features of pupillary areflexia, paralysis of convergence, and strong evidence of involvement of either the left brachium conjunctivum or the right red nucleus. Unilateral ophthalmoplegia with red nucleus involvement (Benedikt's syndrome) and unilateral ophthalmoplegia with bilateral superior cerebellar peduncular involvement (Nothnagel's syndrome) are well-established cerebrovascular syndromes.

Only one case resembling the case reported here has been described in the past 20 years. That was the report in the French literature by Cardona[5] in 1940 who described the case of a 52-year-old "senile" white man who suddenly developed a staggering gait to left and dysdiadochokinesia of the left extremity as well as the typical eye signs

* From the Department of Internal Medicine, Harrisburg Polyclinic Hospital.

TABLE 1

COURSE


Dosage
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Right mydriasis
Able to read
Paralysis of downward gaze
Paralysis right upward gaze
Paralysis of convergence
Cerebellar signs
DISCHARGED
Vitamin B complex 1 cc. bid
Penicillin Procaine 600,000 units bid
Cortisone (Meticortin) 10 mg. qid (tapering off)
Three-month follow-up

Parietal paralysis of convergence still present and double vision on looking to the right. No cerebellar signs.

described by Parinaud (able to perform conjugate deviation to right and left and convergence but unable to perform vertical elevation and lowering of the eyes). The right pupil, as in the case herein described, was dilated and completely areflexic.

Because my patient had blood pressure of 180/110 and a negative blood and spinal fluid Wassermann, it was believed that a vascular lesion involved and obstructed the median supratuberantial arteries of Duret. Disease of these arteries are responsible for Benedikt's syndrome (Claude's). Cardona considered that the additional symptoms of Parinaud's syndrome were due to an extension of the malacia (caused by occlusion of

these arteries) to involve the central fascicle of the peduncular calotte.

Differential diagnosis of this case should be limited to the nuclear and supranuclear ophthalmoplegias because of the unusual association with cerebellar symptoms. According to Alpers,[1] encephalitis, luetic and Wernicke's encephalopathies, tumors of the midbrain and cerebellopontine angles, arteriosclerotic softening, and multiple sclerosis are the outstanding causes of nuclear ophthalmoplegia and, together with traumatic or arteriosclerotic hemorrhage and occlusion, complete the differential list. Because of the afebrile but acute onset and the bilateral involvement in this case, plus the nonalcoholic history, it was possible to narrow the differential diagnosis to lues, multiple sclerosis, and vascular lesions.

According to Walsh,[2] only rarely is there complete internal ophthalmoplegia in multiple sclerosis (one in 150 cases of multiple sclerosis with ophthalmoplegia). Although it is impossible to exclude lues, the final diagnosis was limited to a vascular lesion (hemorrhage or embolism of the basilar paramedial branches) in view of the associated auricular fibrillation and hypertension. The incidence of vascular lesions as the cause of nuclear ophthalmoplegia in 221 cases at the Mayo clinic[3] was reported as 14 percent, although no information as to the course was reported.

The remarkable recovery in this case speaks against a vascular etiology. Anticoagulants were not used because the patient was too remote from laboratory facilities. Meticortin was used because of the report of Russek, et al.[4]; however, as improvement was already noted prior to its use (as well as the use of penicillin), it is impossible to draw any conclusions.

Jefferson Medical College Hospital.

References

1. Alpers, B. J.: Clinical Neurology. Philadelphia, Davis, 1958.
2. Walsh, F. B.: Clinical Neuro-Ophthalmology. Baltimore, Williams & Wilkins, 1947.
3. Rucker, C., Dyer, J., and Smith, D.: Causes of acquired paralysis of ocular muscles. Am. J. Ophth., **41**:951-55 (July) 1956.
4. Russek, H. I., Russek, A. S., and Zohman, B. L.: Cortisone in immediate therapy in apoplectic stroke. Year Book of Medicine. Chicago, Year Book, 1958.
5. Cardona, F.: Inferior syndrome of red nucleus associated with Parinaud syndrome: Case. Riv. pat. nerv., **56**:29-39 (July-Aug.) 1940.

PIGMENTED PAPILLOMA OF THE LIMBUS

Undergoing Malignant Change

B. M. Chatterjee, F.R.C.S.
Calcutta, India

Papillomas are benign new formations, growing from a surface epithelium, consisting of a central fibrovascular core which sends numerous fingerlike processes toward the surface, each supporting blood vessels, the whole being enveloped in a covering of hyperplastic epithelium (Vines, 1949). However thick these epithelial layers may be, they lie upon a basement membrane. An important secondary change in a papilloma is its conversion into an epithelioma when the epithelium begins to invade the tissues beneath it. A papilloma of the conjunctiva generally arises in the conjunctiva or at the limbus, which may be pigmented (Duke-Elder, 1946).

Since papillomas tend to become a squamous-cell type of epithelioma, in some instances it is difficult to say whether the lesion should be classified as a papilloma or a squamous-cell epithelioma (Reese, 1951). Ash and Wilder (1942) classified eight of their 48 epitheliomas of the limbus as papillary squamous-cell type.

Case Report

J. A., a Hindu man, aged 56 years, attended the Ophthalmic Department of the S.S.K.M. Hospital, on February 24, 1959, with the history that about

three years ago he noticed a small swelling at the limbus of the right eye at the 3-o'clock position which had been increasing in size for the last three months. There was no history of pain, bleeding, or discharge from that eye. There was, however, a sense of discomfort.

On examination the right eye showed an irregularly triangular, almond-shaped, elevated and partially pigmented mass, situated at the limbus at the 3-o'clock position, encroaching laterally on the cornea and partially covering the pupillary area and medially on the bulbar conjunctiva (fig. 1). The size of the mass was 1.0 cm. by 1.0 cm. and elevated to such an extent as to protrude through the palpebral fissure, even when the eyelids were closed. The surface of the new growth was irregular and warty and the lower portion of it was darkly pigmented. A horizontal and vertical leash of blood vessels proceeded to the under surface of the growth from the bulbar conjunctiva. The new mass could be lifted up from both the corneal and the conjunctival surfaces and was attached to the limbus by a narrow pedicle. The vision, fundus, and intraocular pressure were normal in this eye.

The left eye was normal in every aspect. The regional lymph glands were not palpable. Systemic examination and laboratory investigations did not reveal any abnormality.

Operation. On March 3rd, the new growth was easily removed by excising the pedicle which was attached to the limbus and the wound was repaired by apposition of the conjunctiva.

On histologic section the tumor showed the structure of a papilloma with papillae consisting of cores of connective tissue covered by several layers of epithelial cells (fig. 2), which invaded the subepithelial tissues at places breaking through the basement membrane. Brownish pigment was seen scattered among the epithelial cells (fig. 3). The microscopic diagnosis was papilloma undergoing malignant change.

Progress. The patient was kept under observation for three months but no evidence of recurrence of the growth was detected.

Discussion

Duke-Elder (1946) has described three types of papillomas at the limbus:

a. Tumors springing from the limbus which do not show a tendency to spread.

Fig. 1 (Chatterjee). The patient with the tumor.

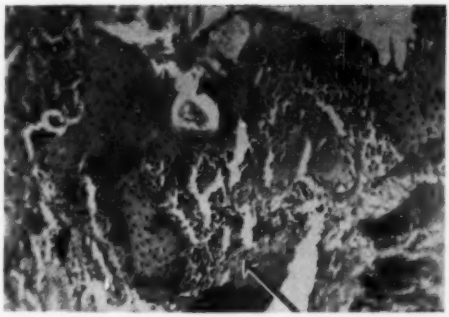


Fig. 2 (Chatterjee). Epithelium breaking down through basement membrane.

b. Tumors beginning on the bulbar conjunctiva near the limbus and spreading toward the cornea.

c. Tumors beginning at the limbus itself and developing entirely in the cornea.

Obviously the tumor reported belonged to the first group. The malignant change was very early and so there was no involvement of the regional lymph glands and there was no recurrence. The scattered pigmentation

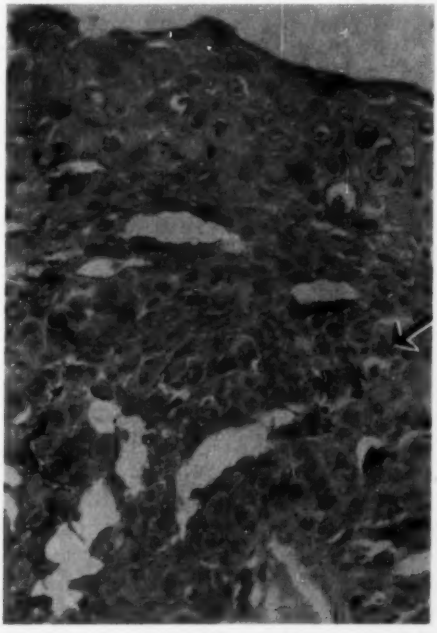


Fig. 3 (Chatterjee). Scattered brown pigment in epithelium.

of the epithelium could not be ascribed to the use of any silver-containing eyedrop. Willis (1953) has mentioned that pigmented papillomas, also called seborrheic keratosis, senile warts, or acanthotic nevi, are common in the skin of middle aged and aged persons. Histologically, the epithelial cells covering these papillomas contain varying amounts of finely granular brownish pigment. These growths have nothing in common with pigmented moles. No nevus cells are present and, when a malignant growth develops, the growth is a squamous-cell carcinoma. The pigmentation of the tumor reported, although rare in occurrence, was similar in nature to papillomas elsewhere.

244, Lower Circular Road.

ACKNOWLEDGMENT

I am indebted to Prof. Ikat, director of pathology of the Institute for Postgraduate Medical Education and Research, for the pathologic reports and to Maj. Gen. A. Gupta, the surgeon superintendent of the S.S.K.M. Hospital for permitting me to publish this case.

REFERENCES

1. Ash, J. E., and Wilder, H. C.: Epithelial tumor of limbus. Am. J. Ophth., **25**:926-932, 1942.
2. Duke-Elder, W. S.: Textbook of Ophthalmology. London, Kimpton, 1946, v. 2, 1977-79.
3. Reese, A. B.: Tumors of the Eye, New York, Hoeber, 1951, p. 27.
4. Vines, H. W. C.: Green's Manual of Pathology. London, Bailliere, Tyndall and Cox, 1949, p. 403.
5. Willis, R. A.: Pathology of Tumors. London, Butterworth, 1953, ed. 2, p. 268-269.

FREQUENCY OF SYMPATHETIC OPHTHALMIA

IN DIFFERENT PARTS OF THE WORLD

ADALBERT FUCHS, M.D.
Meran, Italy

Going over the 367 questionnaires I had received for my book, *Geography of Eye Diseases,* I learned that sympathetic ophthalmia is present everywhere and to the same extent; there are only a few exceptions. According to the numbers given by 351 hospitals we find:

No. Hospitals	No. Cases in One Year
130	0
77	1
40	2
22	3
2	4
10	5
10	6–15
9	Especially high

In 1941 I[1] published statistics of the etiology of 100 cases of sympathetic ophthalmia which I had examined histologically. In 31 percent the disease had followed an operation: 21 percent after cataract extraction eight percent after glaucoma operation, one percent after staphyloma operation, and one percent after extraction of luxated lens.

Since operations seem to be such an important cause of sympathetic ophthalmia I calculated the cases of sympathetic ophthalmia reported in the questionnaires in relation to the number of cases of cataract extraction and glaucoma operations. Below are such figures for hospitals in which more than five cases of sympathetic ophthalmia were recorded:

Lille (France)	151/6
Wroctawin (Poland)	228/9
Istanbul (Turkey)	191/7
Ankara (Turkey)	493/27
Amritsar (India)	2.062/10
Sitapur (India)	3.899/39
Rangoon (Burma)	353/226
Tokio (Japan)	244/11
Lomé (F.W.A.)	225/25
Sud Vietnam	172/8

I was not able to get information on the high incidence of sympathetic ophthalmia in the Moslim Free Eye Hospital in Rangoon, Burma.

Reviewing this list one is astonished to see that big industrial cities show no especially large number of cases of sympathetic ophthalmia, for instance in the United States. Naturally, one surmises that this is due to prevention of injuries in modern industry. However, in countries with a large agricultural population sympathetic ophthal-

mia seems to be rare; for instance Egypt did not note a single case and very few were noted in Spain. Equally few cases were recorded by many hospitals in India where, for instance, one hospital recorded not a single case of sympathetic ophthalmia after 2,000 operations, and in Madras among 59,682 new patients only three cases of sympathetic ophthalmia occurred.

There is considerable difference of opinion concerning the etiology of sympathetic ophthalmia in the United States and in Europe. Nakamura[2] (1932) said that Harada's disease, sympathetic ophthalmia, and uveitis with poliosis, loss of hair and disturbance of hearing belong to the same group and are related to each other. This opinion is now adopted by many ophthalmologists. I also consider these three diseases to be caused by similar types of virus. If, Harada's disease and sympathetic ophthalmia are related diseases one would expect many cases of sympathetic ophthalmia in Japan and China where Harada's disease is common. This is not true. Table 1 shows the low frequency of sympathetic ophthalmia in Japan.

A clinical difference between sympathetic ophthalmia in Japan and Europe and the United States is quite interesting. In Japan, cases of sympathetic ophthalmia are frequently complicated by detachment of the retina, a finding which is exceedingly rare in Europe or in the United States. This seems to indicate that sympathetic ophthalmia in Japan is markedly similar to Harada's disease.

Hamada[3] (1934) found six high retinal detachments among 10 cases of sympathetic ophthalmia; the detachment disappeared after a few months and left a fundus with diminished pigmentation, a frequent finding in Harada's disease. He also mentions that sympathetic ophthalmia frequently begins with headache, tinnitus, increase of pressure, and lymphocytosis of the spinal fluid, alopecia, and poliosis in cases in which there is a sympathetic choroiditis. Such symptoms in cases of sympathetic ophthalmia, are exceedingly rare in Europe. Three cases of Hamada's followed cataract extraction with incarceration of the iris. How common such detachment of the retina is in cases of sympathetic ophthalmia in Japan becomes apparent from the fact that Ishihara[4] includes two pictures of it in his *Atlas*.

TABLE 1

FREQUENCY OF SYMPATHETIC OPHTHALMIA IN RELATION TO THE TOTAL OF CATARACT EXTRACTIONS AND GLAUCOMA OPERATIONS IN JAPAN

Hospitals	Cases	Operations	New Patients a Year
15	0	721	50,029
7	1	544	29,579
5	2	494	16,460
1	3	63	3,533
1	5	92	5,354
1	6	194	9,640
1	11	244	4,576

I tried to get information on the incidence of retinal detachment in cases of sympathetic ophthalmia. Prof. Imachi (Kobe) found it nearly always while Prof Suzuki (Chiba) never saw a detachment. Prof. Umazume (Tokyo) wrote me that one can read in the *Encyclopedia Japonica:* "Ablatio exists in many cases even for a time." Prof. Dodo (Hiroshima) saw a case with a very high detachment; detachment is, however, not the rule.

In Taiwan, Dr. Ho-Ming Lin did not see a single case in six years; nor did Dr. Wilson in New Zealand.

Dr. Banaji (Bombay) has never seen a detachment in a case of sympathetic opthalmia while Dr. B. K. N. Rao (Bangalore) wrote: "Yes, we do have retinal detachment in some cases of sympathetic ophthalmia. These form a small part of all detachment cases due to various causes (traumatic, myopic, etc.)."

There is quite a wide difference in the clinical incidence of sympathetic ophthalmia in different parts of the Western World and the United States and of certain areas of Asia. It would be interesting to follow this difference and to study the relation between sympathetic ophthalmia and Harada's disease.

Karl Wolfstrasse 14.

REFERENCES

1. Fuchs, A.: Med. Welt, **15**:294, 1941.
2. Nakamura: Klin. Monatsbl. f. Augenh., **89**:46, 1932.
3. Hamada: Acta Soc. Ophth. Japan, **38**:173, 1934.
4. Ishihara: Atlas of the Fundus Diseases. Figs. 148, 149, 150, 152.

AN EYE-DRESSING TRAY

Y. A. STATON, M.D.
West Palm Beach, Florida

The eye-dressing tray described here was developed with the primary purpose of avoiding contamination and preventing cross infection. Six months use in the Good Samaritan Hospital has revealed other advantages. It is convenient and time-saving for the physician. It conserves time for the nurses on the ward, the personnel in the central supply room, and the pharmacists. It is believed that it will ultimately prove economical since its use avoids discarding medications that was necessary to provide fresh sterile solutions on the eye-dressing trays formerly in use.

The stainless-steel shell with cover is a standard syringe sterilizing tray minus the usual insert. The special insert was manufactured of stainless steel by a local sheet metal shop. The forceps container and stainless-steel ointment jars are standard equipment. The glass containers for cotton-tipped applicators and solutions are standard drug-room supplies.

The tray contains a thumb dressing forceps, a curved pointed suture forceps, a serrated toothless suture forceps, 2.0 by 2.0 gauze squares, cotton-tipped applicators, eyepads in sterile envelopes, 0.5-inch adhesive and 0.5-inch plastic tape. Solutions included for extraocular use are 70-percent alcohol and whisk, an adhesive remover.

The only solution for ocular use contained on the tray is a 15-cc. plastic squeeze bottle of sterile saline sealed in a hard plastic container. No other medication is included on the tray. After removal of the solutions and adhesive and plastic tapes, the entire tray can be sterilized as a unit.

The physician includes an order for the tray in the postoperative orders. At the same time he orders medications he expects to use in postoperative dressings. Ointments that are ordered come from the drug room in their usual containers sealed with plastic tape. Solutions that are ordered are 5.0-cc. portions in sterile plastic squeeze bottles sealed in hard plastic containers.

The tray is kept covered at the patient's bedside throughout his stay in the hospital and is never used for any other patient. The medicaments are placed in the patient's medicine shelf at the nursing station. After opening and use they are kept on the dressing tray at the patient's bedside. Unopened packages are returned to the pharmacy upon the patient's discharge from the hospital.

Ten such trays have proved adequate to date to service this 230-bed general hospital.

1717 North Flagler Drive.

ACKNOWLEDGMENT

The following members of the staff co-operated in the development of this tray: Drs. John A. Failla, William Gernon, John B. Nicholson, Raymond R. Preefer, William Y. Sayad, and L. R. Teasdale.

Fig. 1 (Staton). The eye-dressing tray.

OPHTHALMIC RESEARCH

EDITED BY FRANK W. NEWELL, M.D.
950 East 59th Street, *Chicago 37, Illinois*

Abstracts of papers presented at the meeting of the Mid-Southern Section of the Association for Research in Ophthalmology, Inc., Fort Worth, Texas, November 11 and 12, 1960.

Samuel B. Johnson, M.D., *Section Secretary*

The coefficient of scleral rigidity: Effect of variation of the intraocular volume. Whitney G. Sampson, M.D., and Louis J. Girard, M.D., Division of Ophthalmology, Baylor University College of Medicine, Houston, Texas. (This work was supported by a grant from Knights Templar Eye Foundation.)

Although the influence of the initial volume on pressure-volume increments in the eye has been known for some time, the most widely used relationship between pressure and volume changes within an eye, Friedenwald's coefficient of scleral rigidity, omits consideration of it entirely. This coefficient of scleral rigidity was used by Friedenwald as a measure of the structural rigidity of the eyeball. Accordingly, eyes having a high value for this coefficient were considered to have a greater resistance to deformation due to an increased structural rigidity in their walls. Conversely, eyes having a low value for this coefficient were more structurally pliable and hence would show less resistance to deformation. In arriving at his formula, Friedenwald assumed the initial volume of the eye to be roughly constant and dealt only with increments of volume and their effect on the intraocular pressure. Our work and that of other investigators suggest that this assumption is unwarranted and indicates that the present formula of Friedenwald for the coefficient of scleral rigidity, as a measure of the structural pliancy or rigidness of the ocular coats, is unsound because it omits the initial intraocular volume as a variable.

This study presents experimental data on pressure-volume relationships in cat eyes of varying initial intraocular volumes. The eyes were cannulated through the anterior chamber with a 23-gauge needle and volume increments injected with a microliter syringe. The pressure changes induced by these volume increments were measured with a strain gauge and a suitable recording apparatus. The data were analyzed first with Friedenwald's formula and an inverse relationship between initial volume and coefficient of scleral rigidity was found. When the data were reanalyzed using a modification of Friedenwald's formula which considered the volume increment as a percentage of the total initial volume of the eye, a tendency toward a uniform coefficient of rigidity (the volume corrected scleral rigidity) was demonstrated.

The results of this study and the work of others suggest that the effect of the structural pliancy or rigidness of the scleral walls on the coefficient of scleral rigidity as calculated from Friedenwald's formula, when measured over normal pressure ranges, is of less significance than was previously thought. On the contrary, variations in the initial intraocular volume seem to constitute the most important single factor in the variation of the coefficient of scleral rigidity between normal eyes. The variation in intraocular volume is therefore not a factor apart from the coefficient of scleral rigidity but an integral variable in its makeup when calculated according to Friedenwald's formula. Friedenwald's assumption of a roughly constant initial volume of the eye in arriving at his relationship for quantitating the structural rigidity of the ocular coats is therefore definitely unwarranted, and many of the corrections for scleral rigidity used in clinical ophthalmology during tonometry and tonography are not correcting for differences in the structural pliancy of the scleral walls but in effect are adjusting for variations in the initial intraocular volume. As a consequence, these variations in initial volume must replace many of those attributed to the structural pliancy of the scleral walls which to date have been held almost entirely to account for discrepancies between the findings of applanation and indentation tonometry.

Saline versus balanced salt solution in intraocular surgery: A double blind study. C. A. Struve, M.D., T. D. Gage, M.D., D. W. Bishop, M.D., and R. L. Rock, M.D., Division of Ophthalmology, Department of Surgery, University of Texas Medical Branch Hospitals, Galveston, Texas.

This work is a clinical study of the effect on the cornea of saline and balanced salt solution when used as an irrigating solution in intraocular surgery.

In 50 consecutive cataract extraction operations 5.0 cc. of an unknown irrigating solution (saline or balanced salt solution) were used in each case. Postoperatively the amount of reaction was graded in terms of striate keratitis and haze. Also the day for complete clearing was noted.

The results show a very slight difference between the two groups with respect to corneal haze and no statistically significant difference in the incidence of striate keratitis. An average of 4.13 days with a standard deviation of 2.05 days for saline and 3.46 days with a standard deviation of 1.60 days for balanced salt solution was required

for the cornea to clear. Statistical analysis revealed a P value of 0.30.

It is concluded that there is no marked obvious difference in the cornea following the use of saline instead of balanced salt solution in cataract extractions. Any possible special advantage of balanced salt solution for this purpose remains to be demonstrated.

Treatment of retinoblastoma by fractional intra-arterial TEM and irradiation. Joseph P. Rumage, M.D., New Orleans, Louisiana.

Analysis of cases of retinoblastoma at Charity Hospital treated prior to 1959 with simple enucleation or enucleation combined with x-radiation showed that the stage of the disease at time of therapy was more significant than the type of therapy administered in determining the fate of the patient.

Encouraged by the work of Reese who added triethylenemelamine (TEM), six consecutive cases of retinoblastoma have been treated with enucleation followed by fractional radiation and intra-arterial TEM. The total tumor dose approximates 2,500 r. The TEM is delivered into the internal carotid artery through a tube placed through the superior thyroid artery into the external carotid artery. TEM is given in 0.3 mg./kg. doses over a two-week period. All the patients are alive and apparently free from disease at this time.

It is recommended that a patient presenting with a small, localized unilateral tumor should have simple enucleation. A large lesion, or one with extraocular spread should have enucleation followed by fractional TEM and radiation. A patient with bilateral tumor should have enucleation of the more involved eye and TEM and x-radiation to both sides to save the other eye.

Continued success with this therapy may eventually lead to treatment of a small, localized tumor with X-rays and TEM, leaving surgery as a last resort.

Treatment of herpes simplex keratitis with copper sulfate iontophoresis: A preliminary report. Stuart I. Brown, M.D., and Monte G. Holland, M.D., Department of Ophthalmology, Tulane University Medical School and The Eye, Ear, Nose and Throat Hospital, New Orleans, Louisiana.

Thirteen patients with disease ranging from dendritic to dendritic and stromal to keratoconjunctivitis with severe uveitis were treated by iontophoresis with copper sulfate. With the exception of one patient whose milliamp minutes of treatment was homeopathic and one with a chronic bacterial conjunctivitis associated with a dendritic keratitis, all patients improved with no evidence of viral disease in one week's time. It is believed that this form of treatment would be useful in the treatment of herpes simplex keratitis, especially in those cases with stromal involvement.

Ocular distensibility as a function of temperature. Monte G. Holland, M.D., Bruce Tischler, B.S., and Joseph Bellestri, B.S. Department of Ophthalmology, Tulane University Medical School, New Orleans, Louisiana.

In previous studies we have presented our technique for the measurement of the ocular distensibility of the enucleated cat eye and a mathematical formulation of the ocular rigidity function based on empirical curve approximation analysis, utilizing a digital computer. In the reported technique the importance of temperature control is emphasized. The present investigation deals with the measurement of the ocular distensibility at several temperatures ranging from 7.0°C. to 37°C.

Statistical analysis of the data shows that the distensibility varies significantly with the temperature and in the expected direction, that is, the distensibility is less at lower temperatures. The most significant change occurs between 27°C. and 37°C. The importance of these results to the measurement of distensibility in the living and enucleated eye is discussed, as well as the relation to determinations of aqueous flow in the experimental animal at different temperatures.

Dinitrophenol-induced cataracts in the Avian embryo: 2.—further studies. G. L. Feldman, Ph.D., Fay A. Doyle, B.A., J. P. Abbott, M.D., and L. J. Girard, M. D., The Methodist Hospital, Houston, Texas. (This study was supported in part by Public Health Service Grant No. B-2297 from the National Institute of Neurological Diseases and Blindness, and in part by Grant No. NSF-G10845 from the National Science Foundation.)

Previous studies have shown that the chick embryo was susceptible to dinitrophenol-induced cataracts after the eighth day of incubation. The susceptibility was found to decrease after the 12th day and declined to zero by the 15th day. Further studies were initiated to (1) ascertain whether dinitrophenol had a pathologic effect on other tissues, (2) provide more information on the mode of dinitrophenol action and, (3) obtain metabolic parameters associated with embryonic development with which to correlate the pathologic effect of the drug.

The drug was found to be highly specific for the lens in its pathologic effect. The cataractogenic effect and toxicity of dinitrophenol depended on the ionic form in which the drug was administered. The phenolic form produced more cataracts with less mortality than did the sodium salt. The decreasing susceptibility towards dinitrophenol-induced cataracts correlated well with the development of the adipose tissue which was found to exhibit very high lactic dehydrogenase activity. This enzyme as well as malic dehydrogenase also increased in the whole embryo during this period. The development of the adipose tissue was accompanied by gradually increasing levels of neutral lipid, particularly triglyceride.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

April 6, 1959

DR. ARTHUR LINKSZ, *chairman*

Panel discussion on "Ocular physiology in clinical practice." PANEL: Dr. Francis Heed Adler, Dr. Albert M. Potts, and Dr. Alfred Kastenbaum. MODERATOR: Dr. Arthur Linksz.

DR. ARTHUR LINKSZ: This is the 179th regular meeting of the New York Society for Clinical Ophthalmology. A few months ago I went to the New York Philharmonic and Mr. Bernstein, the conductor, also played the *Rhapsody in Blue*. Tonight, somehow, I am in the same role, in that I am the moderator and also one of the soloists. Of course, I wouldn't be as young or half as talented as Mr. Bernstein.

The first question, directed to Dr. Adler, is in two parts:

Should tests for depth perception be included in the visual requirements for a driver's license? What factors must be taken into account in determining the minimum visual acuity compatible with granting a drivers license?

DR. ADLER: Dr. Linksz, let me say at the start that these two questions are loaded. I know they are loaded because I posed them, and with a purpose. You may know that throughout the United States there has been a growing emphasis on traffic accidents and the governors of a number of the states, including Pennsylvania, have appointed commissions to study these accidents; on the commissions are men who have to do with eye care. Unfortunately, these committees are composed of both ophthalmologists and optometrists. I am the present consultant to the committee in Pennsylvania and these questions were sent in by me because of the feeling that ophthalmologists are in no position to give the answers to the heads of the commissions until they get together and make some decisions among themselves as to what these answers should be. The groups of nonmedical practitioners have done just that and have sent in to the committee answers which are imposing but of questionable validity.

Now the questions which you are going to have to work out among yourselves are: "What factors in vision are necessary, what standards are necessary for examinations to license individuals to drive private cars?" Various governors throughout the United States are attempting to set such standards.

We must break down all visual functions into their component parts, and decide among ourselves which of these are the most important and what standards for each we must set. It would seem all of this should begin with visual acuity and obviously we would insist on testing central acuity first.

What level of central acuity should be set as the standard below which an individual should not be encouraged nor permitted to drive? So far the committees throughout most of the states and in Pennsylvania, for which I speak, have accepted as minimal a visual acuity of 20/40 in each eye, or in the better eye, to pass without further examination.

The optometric group wants vision of 20/20 as the only acceptable and a referral to either an optometrist or ophthalmologist if the visual acuity is below 20/20. That means that, in order to be allowed to drive, all persons whose vision is below 20/20 will have to be fitted with glasses. Most ophthalmologists and the various committees feel that is reductio ad absurdum and are settling for a visual acuity of 20/40 without further examination. An individual who has a visual

acuity in the better eye of 20/40 to 20/70 must find out if his visual acuity can be brought up with glasses. With vision below 20/70, at the present time, an individual is discouraged for driving. The one-eyed individuals and those who are aphakic, pose special problems.

The second important factor to consider is the extent of the visual field. At present it is generally agreed that, if the binocular visual field is 140 degrees, the individual will pass; if it is 110 degrees and below, he would not be permitted to drive. Concentric contraction of the visual field in cases of glaucoma, homonymous hemianopia, and similar conditions pose serious safety problems.

There is much talk on depth perception and little agreement as to what standards should be set or what tests should be applied. Most individuals, even those with one eye, acquire very good depth perception although they lack stereopsis, which is depth perception by parallax. The monocular clues afford them enough depth perception so that in ordinary driving tests they succeed well in passing cars and cutting in and out. Should we insist on stereopsis? That is a question that has to be answered.

Probably more important than depth perception and certainly far more important than stereopsis, which is really only little employed at ranges used in passing vehicles, is the judgment of speed. In the early days of aviation stereopsis was a requisite for flying. Everybody realizes today that stereopsis in landing aircraft is of little consequence because the speeds and distances involved are beyond the range where depth perception by parallax is affected. More important is the judgment of the speed of approaching vehicles, a factor which had been tested well in laboratories but, so far as I know, has received little or no attention in driving. An individual has to judge the relative speed of an approaching car to tell whether he has time to cut out of line and in again safely. Tests for this must be developed.

One of the tests which every applicant has to pass is for color vision. Color vision could well go out entirely. I doubt if lack of color vision has ever resulted in accidents. If it does, traffic signals had better be changed, as railroad signals have been changed, from red-green signals to vertical and horizontal lights. They would do a much better job when visibility is poor.

Ocular muscle defects are probably of no moment, except as they cause fatigue. If an individual has diplopia, of course he should not drive.

Finally, there is dark adaptation. In Pennsylvania several individuals were refused licenses to drive at night because the optometrist had put an instrument of their device, called a "glareometer," into the State Police Department where these individuals were examined. If drivers have poor readings from this instrument, their licenses are marked "cannot drive at night." The University of Pennsylvania has obtained a Goldmann dark adaptometer, which is the only standard instrument now on the market, to recheck these individuals.

To summarize: what is needed is an active interest by ophthalmologists in outlining standards which are practicable and reasonable and presenting them to the governors' committees so that visual tests for drivers will not be controlled by nonmedical groups who, unfortunately, seem to have arrived first.

DR. LINKSZ: Thank you, Dr. Adler. I saw the panelists making notes. I would be interested in discussion.

DR. POTTS: One can only add that the experience in Ohio re-emphasizes the difficulties of which Dr. Adler spoke. As long as an automobile is a prestige symbol or an instrument for intimidation, there are factors other than vision which will enter into the cause of motor accidents. However, as physicians, we have to set the standards beyond which an individual cannot drive. One problem is the recent aphakic, the recent monocular individual, who has not yet learned clues for depth perception. What is to be done about him?

Should there be a lapse of time before he is allowed to drive again? As to dark adaptation; the question arises whether the adaptometer in any form measures the ability of an individual to see when driving at night. Does he really use rod vision that is measured on the adaptometer when he drives at night or is he really somewhere in a twilight zone between cone vision and rod vision?

DR. KESTENBAUM: Some people have very good depth perception with one eye. If a man with one eye drives carefully it is better than if a person with two eyes relies on that and drives without care. If dark adaptation could be measured according to our needs and not only according to theory, it would be very important.

What is the time schedule of the development of the fixation reflexes in the infant? What is its practical significance to the clinician?

DR. KESTENBAUM: In order to answer this question one must carefully distinguish between two functions of the eye which are sometimes confused with each other, since both of them are often called fixation. The one function is the directing of the eye to a laterally seen object that attracts attention. This movement toward the object, which takes the image of the object from an area of the peripheral retina to the macula, is preferably called "optically elicited movement" rather than "fixation." This optically elicited movement is a function of the peripheral part of the retina.

Another function is the real fixation which keeps the eyes fixed on an already centrally seen object so that the image of the object stays on the macula. The first function takes the image to the macula, the second keeps it on the macula. The second function, keeping the image on the macula, is a function of the macula itself.

If an object that is fixated is not stationary but moves, the fixating eye is able to follow this object in a movement which is gliding, steady, slow. This movement is called a follow-movement or fixation of a moving object. Such a follow-movement is, therefore, also a function of the macula.

My personal studies started with infants 10 days of age. At the age of 10 days, every child was able to look at a lateral object, that is to perform optically elicited movements, if the object attracted his attention. On the other hand the fixation mechanism which is carried by the macula was found not to be developed until three to six months of age, or, on the average until four months of age. A two-months-old child, for instance, can follow an object only in a series of successive small movements, in a so-called cogwheel movement. At the age of about four months, this movement changes into the steady, gliding "follow-movement." To summarize, the optically elicited movement is present soon after birth, whereas the fixation of a moving object, the follow-movement, develops, on the average, at the age of four months.

The practical significance is as follows: One can take a visual field of an infant almost from birth. One introduces a conspicuous object from different sides into the peripheral field and observes whether the eye reacts correspondingly. If the eye looks toward the object, then obviously the child has seen the object. This test is done in eight meridians of each eye. In this way, one can take visual fields of an infant with a precision of 20 to 30 degrees.

One cannot test the macular function before the age of four months. After four months, one can see whether the child is able to follow an object in a slow steady movement or not. If he can do this, then he has macular vision.

Another method is the use of the optokinetic drum, which causes optokinetic nystagmus. The first phase of this nystagmus is a follow movement and therefore is present only if the macula is developed. If, after four or five months, the eye reacts to the drum with a nystagmus, the presence of central vision has been proven.

DR. LINKSZ: Thank you. Dr. Adler, would you like to add anything?

DR. ADLER: I have nothing to add. I would like to ask Dr. Kestenbaum if optokinetic nystagmus isn't present right after birth. It seems to me that somebody in Boston recently has found that optokinetic nsytagmus is present immediately after birth. I don't quite understand how you test for the function of fixation. I understand following movements and you can get those in the very young infant but how do you test the very young infant for macular fixation? If he does follow something, he does turn his eyes to it. Isn't that fixation?

DR. KESTENBAUM: We have to differentiate between two kinds of optokinetic nystagmus. One form is elicited by a little drum with black and white stripes that is turned in front of the eye. The resulting nystagmus is a function of the macula and, as I could observe, is not present before four to six months of age. Cogan, in Boston, uses another method. He uses a large cylinder that has black and white stripes on the inside and turns around the patient so that almost the entire visual field is filled out by the moving stripes. This cylinder is the original cylinder invented and used by Bárány, the inventor of the test for optokinetic nystagmus. Later, Bárány used the small drum. With the use of such a large cylinder that turns around the patient, and wherein the greatest part of the content of the visual field moves, the peripheral field may also elicit an optokinetic reaction. According to various studies (Smith and Bridgam) the first form elicited by the macula is a cortical reaction, while the second form, elicited by the entire retina, is subcortical.

The second form of optokinetic nystagmus that is elicited by the entire retina, and requiring only the presence of some vision, exists at birth. This form does not say anything about the condition of the, as yet undeveloped, macula. The first form, elicited by the relatively small drum, is not found prior to the age of four months, on an average; it depends on the presence of a well-developed macula. Therefore, the presence or absence of this second form in a child over four months of age permits a conclusion concerning the condition of the macula and of the central vision.

The follow-movement is a slow steady movement that occurs if the eye is already fixed on a moving object. The eye goes with the object. This ability to fix the eye on a moving object is not acquired before the age of four months. Conversely, the ability to look at an object entering the field from the side is a quick movement toward the object. This movement, the optically elicited movement, is present at birth. Follow movement and optically elicited movement are not to be confused with each other.

What recent contributions of basic science to the study of cataract promise to affect the treatment of cataract patients?

DR. POTTS: I am sorry that this question came so early in the program for fear that the answer may give a wrong impression. I am in favor of basic science. It just happens that this particular question demonstrates how difficult it is to attack the problem by laboratory methods.

We know, perhaps, more about the physiology of the lens than about any other of the organoids that constitute the eye. We know a great deal about its chemical composition: that it is extremely high in protein, that the proteins are unique, that there are three principal types of protein. We know a great deal about the amino-acid composition. We know about the presence of sulfhydryl groups in the lens and we know that sulfhydryl groups disappear when cataract comes. We know that the proteins become less soluble or rather the least soluble type of protein becomes predominant in cataract. We know about the presence of ascorbic acid and the fact that it decreases when cataract comes.

We know about the potential across the lens capsule and that it is independent of an underlying epithelium; that the capsule has a

potential either anteriorly where there are epithelial cells or posteriorly where there are none. This ties in with the work of Dr. Dische who pointed out that the lens capsule is a metabolizing machine and not simply an inner membrane, such as one might expect from its histology.

In spite of all these things, we still know very little about cataract. We know that the metabolism of the lens gains most of its energy by the process of breaking sugar molecules in half—glycolysis; that the little bit of oxidation goes along very definite pathways: the tricarboxylic acid cycle and the so-called gluconic acid "shunt." Still, though we know the metabolism decreases when cataract comes, we can't say that inhibition of a particular metabolic process is the cause for cataract. There are two small gleams of light. An old one, one that we have known for some time, has to do with the immunologic specificity of lens protein. It is based on the fact that the lens is organ specific and not species specific so that an individual may become sensitized to his own lens protein. This potential phacoanaphylaxis cautions the physician against bilateral extracapsular extraction done at different times. The other gleam, a more recent one, comes from the laboratory and has to do with minimizing extracapsular extractions by use of a proteolytic enzyme in the anterior chamber to lyse the zonule.

We who work in the laboratory are certain that the answer is going to fall out one day and all in one piece, but from the foregoing it is easy to see that the day has not yet arrived.

DR. LINKSZ: Dr. Adler, would you like to ask any questions or add anything?

DR. ADLER: Is it your conception, Dr. Potts, that these various changes—the disappearance of sufhydryl groups and the ascorbic acid and the changes in the sodium/potassium ratio—precede the formation of cataract or are they merely evidence of death of cells?

DR. POTTS: I think that, with one exception (the drop of glutathione content in the lens), all of these changes occur after some type of opacity is first seen. The change in glutathione content is the only thing that happens just before or concurrently with the appearance of opacity. Even here one can't say which is the cart and which is the horse —which is the causative agent and which is simply a sequela of some unknown cause.

From the point of view of ocular physiology, please compare indentation and applanation tonometry.

DR. ADLER: What I am going to say is purely from the viewpoint of physiology. I am purposely avoiding any comparison of the two methods from the clinical point of view. What are the things in ordinary indentation tonometry which should be avoided and how does applanation tonometry succeed? To begin one has to think of what indentation tonometry does; it indents by a weight a globe which is a semi-elastic capsule. The indentation of the globe changes the internal pressure of the eye before the weight is applied; it increases the internal pressure. The pressure in the eye before the weight is applied will be called P_o and the pressure after the weight is applied is P_t. Since the weights in indentation tonometry are relatively high, there is a relatively great change in volume, which we will call V_c. Schiøtz realized this when he made his first tonometer and made a calibration scale so that P_t would be corrected to give the real pressure before the weight of the plunger, that is P_o, if the eye were of average elasticity. The difficulty is that the volume change (V_c) which results from the application of the weight depends on scleral rigidity, and the volume change is relatively large.

If different individuals have different scleral rigidity, then the P_t values which are read do not represent the P_o values, even though the Schiøtz formula is applied.

In 1940 Friendenwald, recognizing this, worked out the relationship between P_o, P_t, and V_c and what is called a rigidity co-efficient "K" describes the elastic properties of

that particular eye. Nowadays, one can arrive at a fairly correct P_o in cases in which the scleral rigidity is abnormal by taking the readings with two weights, as you know, a 5.5 gm. and a 10 gm. and with Friedenwald's nomogram find out what the P_o really is.

Theoretically this should be satisfactory for all clinical purposes. However, in addition to scleral rigidity there are other factors which make the indentation tonometer not a really accurate scientific instrument.

Recently Olmstead pointed out some of the sources of error in indentation tonometry. One of the errors is due to changes in corneal curvature. Any change in corneal curvature from the average results in a significant change in V_e. Actually, with extreme changes in corneal curvature the P_t readings will be off as much as 30 percent from the actual P_o reading. Of minor importance is the factor that Dr. Olmstead describes as a lifting component force of the tonometer plunger which occurs where the cornea is indented and the factor of the membrane bending around the edges of the footplate which, since different corneas have different facilities of distortion apart from rigidity, introduces still another variance.

To summarize, in indentation tonometry, the following factors tend to give false readings: scleral rigidity, changes of the ocular coat, changes in corneal curvature, changes in the tensile component, lifting the tonometer load and, finally, the bending of the cornea at the edges of the footplate.

The applanation tonometer avoids all these errors because the volume displacement is kept constant. One might say that indentation tonometry applies the principal of constant force and variable displacement, whereas the applanation tonometer applies a constant displacement-variable force principle. The applanation tonometer avoids errors due to changes in volume displacement by keeping the volume displacement constant.

Goldmann made a plexiglass plate which is brought into contact with the cornea by a calibrated spring, the pressure of which is increased until an area of predetermined size is flat and the intraocular pressure P_t is determined as the spring force W over the area. The design of the plate is such that the final volume displacement in the applanation tonometer is kept constant at about 0.44 microliters, whereas the variation with the indentation tonometer is 10 to 20 microliters, quite a significant difference. Therefore, it would seem, that from a theoretical point of view, that the applanation tonometer is a far superior scientific instrument. However, there is one error specific to the applanation tonometer which has to be carefully taken into account, that is the surface tension of the plexiglass plate against the cornea.

Goldmann has eliminated the errors of surface tension by the design of his plate and by covering it with silicon. He uses a specific anesthetic which he believes must always be the same, 0.5 percent Novesin or dorsacaine. He also has rigid instructions on cleaning the plate.

There can be no doubt that the applanation tonometer is superior to the indentation tonometer in avoiding these various factors. It should be useful for checking indentation tonometer readings whenever the Schiøtz readings do not fit in with the clinical picture.

Whether applanation tonometry will supplant indentation tonometry is uncertain. I am sure those who have used it, will agree that it is much more difficult than indentation tonometry. Indentation tonometry is an excellent clinical technique. If we keep in mind that the indentation tonometer was not designed to be a perfect scientific instrument, we won't be harassed too much by changes that throw off our readings.

DR. POTTS: Assuming that ophthalmologists with their delicate skills eventually learn to use the applanation tonometer, I would like to ask Dr. Adler a loaded question. Since not even half of the population sees an oculist with any regularity, should we, after we switch to applanation tonometry (if we do), instead of throwing away our indentation

tonometers, give them to our colleagues in internal medicine so that tonometry will be part of a general physical examination?

DR. ADLER: I don't want us to throw away our Schiøtz tonometers. As to whether the general physician should be taught to use the tonometer, there are two points of view. I personally believe that they should and I am all for it. One argument against this is that there will be too many false positives sent in; I don't object to that. A second argument is that cases with narrow-angle glaucoma will be missed. The pressure will be found normal when there is no blockage of the angle. That is true. However, it seems to me that, if one patient was found on routine physical examination to have high intraocular pressure and subsequently was diagnosed as having glaucoma it would justify encouraging general physicians to take the pressure with a tonometer.

A woman came into my office a month ago and said, "I am worried sick. I have been seeing halos around lights and I've just been reading the *Reader's Digest*." I said, "Madam, half the people coming in here have read the *Reader's Digest* and think they have glaucoma. I assure you that I doubt very much if you have glaucoma. Just don't worry about it. We will take your pressure." Which we did. And she had glaucoma.

Can the development of nystagmus be prevented? What are the physiologic principles involved in your treatment of nystagmus?

DR. KESTENBAUM: The surgical treatment of nystagmus is based on the physiologic principle that a jerking nystagmus increases if the patient looks in the direction of the quick phase of the nystagmus and decreases if he looks in the direction of the slow phase. This principle had been known for many decades for vestibular nystagmus but we found it to be valid for every kind of jerking nystagmus. The indication for surgery is given if jerking nystagmus is present in the primary position and is less in intensity or even absent in another position. The position in which the nystagmus is least or absent is called the "optimum position." The distance between "optimum position" and primary position is measured with a ruler in mm.

The surgical procedure consists of surgical rotation of both eyes in the direction of the fast phase of the nystagmus, in the direction in which the nystagmus becomes *worse*. The extent of rotation equals the extent of the distance, measured in mm., between the optimum and the primary position. In this way, the entire system, including the "optimum position," is shifted to the side of the quick phase to such a degree that the "optimum position" comes to coincide with the primary position. Therefore, after the operation, the eyes show either the least or no nystagmus in gaze straight ahead.

Anderson, in Australia, started from my old concept that, for instance, right nystagmus means a weakness of the gaze to the right, and came to the conclusion that the right-turning muscles had to be strengthened and thus came, independently, to a similar surgical procedure.

Surgical rotation of an eye, for instance, five mm. to the right, is achieved by a five-mm. shortening of the right-turning muscles (right lateral rectus and left medial rectus), together with a five-mm. lengthening of the left-turning muscles (right medial rectus and left lateral rectus). In other words, a five-mm. resection of the antagonist, results in a five-mm. rotation of the eye. Both eyes have to be rotated. If there is also a strabismus, the required surgery for the strabismus has to be calculated along with the measurments for the nystagmus operation.

Can the development of nystagmus in albinism be prevented?

DR. KESTENBAUM: Long ago, I had the hypothetic concept that the nystagmus in albinism is not primarily a hereditary, hence unavoidable, condition, but rather a secondary consequence of the albinism. In my concept, nystagmus is caused by the fact that diffuse, not regularly refracted light passes

through the sclera, the pigmentless choroid, and the pigmentless pigment epithelium, and thus blurs the image produced by the refractive system of the eye in the macular region. Since the macula is not developed at birth but is normally complete at the age of four months, I conceived that the absence of sharp images in this region during the critical first four months, results in maldevelopment of the macula and in nystagmus.

This concept has been based on the fact that bilateral opacities of the cornea following blennorrhea neonatorum (gonorrhea) after birth, almost invariably cause nystagmus, in spite of the absence of any "hereditary factor."

Recently I saw a two and one-half-month-old girl who was born prematurely (seven months), so that she was, according to the schedule, only 14 days old. She showed conspicuously red pupils and severe albinism but no nystagmus as yet. Therefore, I gave her nontransparent goggles, with a central hole of six mm. in front of each eye, so that light rays could not reach the retina through the pigmentless choroid and retina but could only enter through the pupils. In this way, the diffuse light was excluded and only regularly refracted light was admitted so that sharp images were formed in the macular regions. It was important that the distance between the two holes in the goggles equalled the interpupillary distance. The child wore these goggles up to the scheduled age of four months (actually six months) until development of the macula could be assumed. Now the child is about 16 months of age and can look at an object steadily without movement. Only if the child looks to the side or is not attentive, are there irregular nystagmus movements. Of course, one case is not a definite proof, even if the albinism was severe.

I would advise that every newborn child with "red pupils" be examined by an ophthalmologist for albinism. If albinism is established, the child should immediately be given the goggles described, with six-mm. holes, and wear them for a period of four months. Perhaps in this way, nystagmus in albinism could be prophylactically eliminated.

DR. POTTS: I am intrigued with Dr. Kestenbaum's theory of excess light being responsible for lack of macular development. There are reports about absence of light being responsible for lack of development of visual cells but are there other anomalies, such as congenital aniridia, where excess of light causes lack of macular development?

DR. KESTENBAUM: There are several conditions. In adults who work in coal mines under poor illumination and with a lack of sharp contours and the formation of unsharp images on the macula for a long period of time, nystagmus may develop.

The common factor in all these conditions is the presence of blurred images but not complete absence of images in the macular area. The importance to vision of sharp images on the macula can also be proved by other experiments.

DR. ADLER: Doesn't the operation have the same effect as if the patient turned his head? One can then test before operation whether his vision is better. I wonder why he doesn't learn to turn his head?

DR. KESTENBAUM: Very often children who have asymmetric nystagmus learn by themselves to turn the head in the direction of the quick phase of the nystagmus, sometimes in the form of torticollis. The compensatory movement of the eyes takes them to the optimum position. The fact that the vision in the rotated position of the head where the nystagmus is absent is much better than in straight-head position where nystagmus is present proves that the nystagmus is responsible for the torticollis. But the torticollis itself is usually the reason why the patient seeks the physician's help, and the disappearance of the torticollis as a result of the nystagmus operation is an important part of the achievement.

What are Haidinger's brushes? What is their significance for pleoptics?

DR. LINKSZ: Pleoptics is a new word

introduced a few years ago in Europe. It designates a method for the improvement of amblyopia. The generally accepted method up till now consisted in covering the good eye to make our patients use the poorer eye. Some of them were cured in this manner, others were not. Some children seemed to have the innate ability to fixate and to have good visual acuity and for some reason do not get around to use their fovea, whereas in other children there is, apparently, some structural or other kind of deficit of the macula, so that they can be improved by occlusion of the other eye.

The ability of the eye to recognize polarized light was discovered by Haidinger more than 100 years ago, and the entoptic phenomenon elicited by polarized light has since been called Haidinger's brushes. One should actually see these brushes looking at the sky, but this is not easy, due to the fast adaptation of the retina.

Dr. Max Goldschmidt of New York some years ago invented an instrument in which a small motor rotates a polarizing filter in front of a light and, since the filter rotates, the polarized light hits the retina in constantly changing directions as the brushes rotate. The direction of these brushes can only be recognized by the fovea and its surroundings, since only in this part of the retina is there a kind of analyzer of polarized light. According to a generally accepted, though not proved, theory it is Henle's fiber layer which acts as such an analyzer. Dr. Goldschmidt believed that if a child does have a normal macula it will recognize Haidinger's brushes even if amblyopic. If the child does not have a potentially well-functioning macula it will not recognize the brushes. He thought it would be worthless to treat amblyopia in a child who does not recognize Haidinger's brushes.

Our ideas have changed to a certain extent. Both Bangerter in Switzerland and Cüppers in Germany believe that the reasons for the failure of occlusion treatment of amblyopia are different. They believe that some children do not fixate with their fovea but with an extrafoveal area. They believe that amblyopia will improve by covering the good eye only in cases in which foveal fixation ability exists to begin with. In children whose fixation is eccentric, covering of the good eye will not only make things no better but will actually make them worse by reinforcing fixation with the wrong area.

Pleoptic treatment is based on this new idea about the significance of eccentric fixation. This raises two practical points: First, it will be necessary in the future to diagnose the existence of centric or eccentric fixation in the amblyopic eye. This is done with an instrument called the Visuscope, a kind of ophthalmoscope with the help of which both the examining doctor and the patient can at the same time fixate the same target and the examining doctor is able to see with which part of the retina the patient is fixating.

Once the condition of eccentric fixation has been established the pleoptic theory urges occlusion of the amblyopic rather than the good eye, thus to break that habit. Treatment is started later. The essence of pleoptic treatment is to teach the amblyopic child to recognize the position of its own fovea. This is done first with an after-image method, about which there is no time to talk and then by using Haidinger brushes. The new instrument is much the same as Dr. Goldschmidt's but it now serves therapy more than diagnosis. The children learn, by concentrating on the rotating brushes, to fixate what is or seems to be imaged in their fovea. Of course all of this is very new and as yet quite controversial. I am sure you will hear a lot about it in the future.

DR. ADLER: How early can this treatment be started? At what age?

DR. LINKSZ: That depends on the intelligence of the child. Surely not much before five or six years of age. On the other hand it can be used regardless of how old a patient may be.

DR. ADLER: In other words, it is about

the age at which one doesn't hope to get much, if any, improvement by patching the good eye; or if the eye is patched, vision falls off again.

DR. LINKSZ: We are only starting pleoptics in the United States and I don't know anybody yet who has collected sufficient experience. They are ahead of us in England. As a matter of fact when I was in England two years ago they already had a pleoptic clinic at Moorfield's. Their reports are at least encouraging.

Do the toxic amblyopias have a significant physiologic factor in common?

DR. POTTS: I think this could be answered in a single word but to add a little understanding to the answer one ought to consider what one means by toxic amblyopia. Initially gutta serena was a disease entity. When one couldn't see a cataract in a patient's eye and yet the individual could not see, this was a disease entity in preophthalmoscopic days. When the ophthalmoscope became available and fundus lesions could be observed, all diseases which gave visible fundus findings were subtracted from this entity. As a result of this, "amaurosis" and "amblyopia" applied only to those diseases in which no fundus lesions could be seen.

The significance of "toxic" a century or less ago was much different from now. This, too, was a wastebasket category and anything that could not be explained on the basis of systemic disease was considered toxic. In "toxemia of pregnancy" we have a relic of this terminology.

Since the toxic amblyopias represent a subtractive category one wouldn't expect them to have a lot in common and, if one examines the etiology, this is perfectly true. The entity, tobacco-alcohol amblyopia, which was considered a toxic phenomenon up until relatively recently, has been demonstrated fairly conclusively by the work of Carroll and others actually to be a vitamin deficiency. Findings in it correspond in great measure to central scotomas caused by vitamin deficiency, as in cases of prisoners in concentration camps.

Methanol poisoning, another toxic amblyopia, turns out to be a systemic disease in which presumably the ganglion cell layer of the retina is selectively affected. In the case of lead poisoning, which is considered another toxic amblyopia, there are two distinct entities, one a central amaurosis which seems to have to do with the visual cortex and another a retrobulbar neuritis.

A new contribution which has to fall into this category because the category is already established is NP-207 in which the effect seems to be on the pigment epithelium and the etiologic mechanism actually seems to be allergic. This drug was never released to the market but early tests resulted in a few cases of blindness which showed pigmentary changes in the retina.

Still in this category are the results of administration of LSD and Mescaline which, on the basis of optic-nerve section studies, certainly seem to require the participation of the central nervous system in order to elicit their hallucinatory effects on vision.

In the toxic amblyopias, one is dealing with a wide selection of very slightly related and unrelated conditions which, on the basis of our newer knowledge of pathology and chemistry, could perhaps better be given separate and individual names.

DR. KESTENBAUM: I think we have to be careful not to eliminate the word tobacco amblyopia altogether. I think it is a shift in the form of diseases and is not identical with what is now called a vitamin deficiency. We had in Vienna an involuntary experiment of great interest. Before the First World War there were so many cases of tobacco amblyopia at the clinic that we made what is now called a project of it. It was learned that a certain strain of tobacco would produce more tobacco amblyopia than others. After the World War, when there was nothing to eat in Vienna and nothing to smoke, there was not one case of tobacco amblyopia. I am sure that after the war there

was much more lack of vitamins than before the war. Therefore, I don't think that we should completely eliminate tobacco.

DR. POTTS: The question of tobacco amblyopia has been batted around for a good hundred years and one questions the entity today when (at least up to recent information about carcinoma of the lung) there was much more smoking than previously and still no incidence of tobacco amblyopia. In certain vicinities only cigarette smoking is supposed to cause tobacco amblyopia; in other vicinities only cigars or only pipes, and no one has been able to correlate amount of tobacco or amount of nicotine with the incidence of tobacco amblyopia. Perhaps we are talking about a specific vitamin deficiency, particularly among the soluble B-vitamin group, and it is conceivable that this vitamin was in adequate supply in the situation you mention, even though others were not.

DR. KESTENBAUM: Perhaps I should add that most cases of tobacco amblyopia were in smokers who smoked cigars which are not sold in the United States. Then nothing came and then after that was pipe smoking. After a long time came cigars. Almost never did a cigarette smoker get amblyopia. Cigarettes changed the kind of smoking; that may be the reason there is much less amblyopia from tobacco.

DR. ADLER: May I ask Dr. Potts if there is any significance in the fact that this disease used to be called tobacco-alcohol amblyopia and it is only the British who insisted that the alcohol had nothing to do with it. Do you agree with that?

DR. POTTS: This is another instance which may be used to cite the evanescent nature of disease. In Great Britain there never has been alcohol amblyopia. In the United States there has never been any significant amount of tobacco amblyopia. The term resulted from the common symptoms presented by the two groups. One thing which these two groups may have in common (at least up to the time of fortification of foods, which is very significant in this connection) is the possibility of poor nutrition.

DR. LINKSZ: You mean the lack of vitamins in both conditions?

DR. POTTS: Yes.

Is the mechanism for vergences different from that underlying versions?

DR. ADLER: I believe it is and I think the evidence of that is in terms of clinical pathology rather than anything that we know physiologically. As a matter of fact while we do know physiologically something about the oculogyric pathways for versions, as far as vergences go we have no idea where they come from until the innervation reaches either both medial recti simultaneously or both lateral recti simultaneously. The evidence for the separation of versions from vergences must rest entirely on clinical data.

What is that data?

Cases of internuclear paralysis support the belief that the mechanism for convergence is different from that which innervates the medial recti in versions. When an individual with a typical internuclear paralysis looks to the right, the right eye moves to the right, but the left eye will not move beyond the midline, and so you say that the individual has a paralysis of the left medial rectus muscle. But when you ask him to converge, both eyes move in equally, in binocular adduction, which proves that the left medial rectus is not paralyzed when it comes to the innervation for convergence but acts as if it were paralyzed in versions because the pathway for versions is interrupted. Similarly in divergence paralysis. You know that it has been claimed by many that divergence paralysis, like the giraffe, just doesn't exist.

The trouble with divergence paralysis is that many of these cases are seen but not diagnosed. They are mistaken for cases of bilateral lateral rectus paralysis. I believe there is a very definite entity called divergence paralysis which, if the clinical criteria are properly applied, can be diagnosed and

can be diagnosed only when these criteria are applied.

What are the criteria?

One essential is an increasing amount of homonymous diplopia as the test light recedes from the individual. However, when the test light at any one distance is carried around in the arc of a circle, using that radius to describe the arc, the separation of the double images remains the same on both sides as it does in the center. That definitely separates a case of divergence paralysis from a case of bilateral lateral rectus palsy in which not only would the diplopia increase as the light was drawn away from the patient but the separation of the images would increase on moving laterally in version, showing that, in the case of true divergence paralysis, the lateral recti are receiving insufficient innervation in divergence and do not receive a normal amount of innervation for abduction. The cases which have come to post mortem have shown that the lesion causing divergence paralysis is situated in the midline. It has also been noted that, in many cases of divergence paralysis, a paralysis of one lateral rectus muscle develops later on, as the condition progresses. Why? Because the lesion affecting the pathways for divergence is in the midline between the sixth nerve nuclei. In the majority of these cases, when the pathologic process is due to a neoplasm, the growth of the tumor occurs on one side beyond the midline and encroaches onto the adjoining sixth nucleus. Those two bits of evidence prove conclusively that the pathways for vergences and version are separate. I am sure that Dr. Breinin is going to give physiologic evidence for such a belief in the not too distant future.

Dr. Linksz: The question is asked: Of what value is the concept of "nervo-machanism" and proprioception in relation to extraocular muscle imbalance?

Dr. Adler: The person asking this question had specifically proprioception in mind and therefore my answer is to the question:

How great a part does proprioception play in the control of eye movements in man?

First, what is meant by proprioception? To some people proprioception means a very vague sense of or a very vague type of information that is sent into the central nervous system which controls the tension of muscles. To other people proprioception when applied to the eyes means the conscious knowledge of how the eyes are situated in their own orbits and is a serviceable source of information in terms of their own space perception, that is, egocentric localization. If one takes the latter definition of proprioception, the answer is there is very little proprioception in man.

Most of the information for man's space localization comes from visual clues and not from proprioceptive feed-back from the ocular muscles. The evidence for this has been well documented by many people including Dr. Kestenbaum, Dr. Linksz and Dr. Breinin.

We do not know the position of our eyes in the orbit when they are moving in nystagmus. We are aware that they are moving. If we have any sense of movement at all it is that the surrounds are moving and not our eyes.

If the conjunctiva is cocainized and the eye passively moved with a pair of forceps, in the dark, the subject has no knowledge that his eye is being moved as long as he cannot see what is going on. Therefore, it can be said that, in all passive movements of the eye produced reflexly or mechanically, there is no proprioception which creates a sensation of the position of the globe in the orbit. The sensation of a change in position of the eyes only comes about when the individual voluntarily moves his eyes. The information of the position of the globe in the orbit as a result of voluntary versions and vergences is a position sense acquired by the will, if we may use that term, for example when the eyes are voluntarily moved. On the other hand it is known physiologically that there are certainly impulses which are

sent back into the central nervous system when the ocular muscles contract.

Dr. Breinin has shown that very beautifully in electromyographic responses. When the eyes are in the primary position, there is a constant level of innervation being sent into the central nervous system so long as the ocular muscles are attached to the globe. If the muscles are freed from the globe, that innervation ceases. The tension of the muscles creates the message which is sent into the central nervous system. Dr. Breinin found no increase in the message with putting increased tension on any of the muscles, suggesting that there is a limited type of message which is sent from the muscle as the result of that sense.

For years it was claimed that there was no anatomic basis for proprioception in human ocular muscles. For some strange reason man, monkeys, the white-tailed gnu and goat have muscle spindles and physiologists have recorded those messages going into the central nervous system. We have to admit there is proprioception in man but that it probably plays a small part in our knowledge of the position of the eyes in the orbit and of our space perception.

How would you differentiate between ptosis due to levator paresis and ptosis due to involvement of the sympathetic nervous system?

Dr. Kestenbaum: Up to a short time ago, the main possibility of differentiating between the two kinds of ptosis, the sympathetic and the levator ptosis, was, besides the history, a difference in the pupil. If the pupil on the side of the ptosis is wider, one assumes oculomotor paresis; if the pupil is narrower, sympathetic paresis is probable.

I tried to develop another way for differentiating between the two kinds of ptosis. Allow me some anatomic remarks. The levator palpebrae superioris, supplied by the third nerve, runs forward above the superior rectus and spreads out to form its aponeurosis. The aponeurosis does not insert at the convex edge of the tarsus but, united with the orbital septum, it inserts at the anterior aspect of the tarsus. From the inferior aspect of the levator, a smooth muscle originates which inserts at the convex margin of the tarsus, and thus forms a kind of second tendon of the levator. This smooth muscle, the superior tarsal muscle of Mueller, is supplied by the sympathetic nerve. In this way, the tarsal muscle is shortened in high sympathetic tonus and is lengthened in low sympathetic tonus.

This causes an effect that is almost unique in the anatomy of the human body. One has to use the width of the lid fissure as a part of the facial expression; a high sympathetic tonus should be indicated by a wide lid fissure; a low sympathetic tonus should be indicated by a narrow lid fissure. In this way, the width of the lid fissure should serve to communicate to others the height of the sympathetic tonus present.

If one looks upward, the levator works more, and the lid fissure goes up; if one looks down, the lid fissure goes down.

If a patient with a levator ptosis of one eye looks upward, whereby the levator of the lid should co-operate, the ptosis will become more conspicuous. In other words, in the field of action of the paretic muscle, the difference between the two lid fissures becomes greater. If the patient looks down, whereby the levator should relax, the difference between the two eyes becomes smaller.

Conversely, in sympathetic ptosis, in which only the "tendon" is elongated, the levator muscle itself being normal, the lid fissure is always narrower on the side of the paresis than on the other side and the difference between the two eyes remains more or less unchanged, whether the patient looks up, straight ahead or down. The lid fissure shows a behavior analogous to that of strabismus. In paralytic strabismus, due to palsy of an eye muscle, the angle of strabismus varies with the direction of gaze, the degree of strabismus increases in the field of action of the paralytic muscle. Conversely, concomi-

tant strabismus does not alter essentially in different directions of gaze. Therefore, the behavior of the lid fissure, characteristic of sympathetic ptosis, may be called "concomitance sign."

Conclusively, change in the difference between the two lid fissures in gaze up and down, respectively, indicates levator paresis; a more or less unchangeable difference indicates superior tarsalis paresis.

A number of different disease entities cause retinal pigment changes which are ophthalmoscopically indistinguishable from retinitis pigmentosa. How can physiologic knowledge and techniques aid in the diagnosis of these entities?

DR. POTTS: One might add actually to this that there are diseases which cause no retinal pigment change but are clinically indistinguishable from retinitis pigmentosa, and are there physiologic methods for distinguishing all of these? This is perhaps the field of the greatest triumph of electroretinography. Electroretinography promises many things and some of these promises have not yet been fulfilled. The finding that, when a light is shone into the eye, there is an electric current from the eyeball which corresponds in certain respects to the intensity of the light that was shone into the eye, led us all to hope that this would prove a diagnostic tool—like the electrocardiogram—of tremendous power. Perhaps this may still be true.

Certainly one may say that in the differentiation of retinitis pigmentosa, retinitis pigmentosa sine pigmento and retinitis punctata albescens—all of which sometimes run in the same hereditary line—from pseudoretinitis pigmentosa, seen in the case of syphilis, or generalized chorioretinitis due to other causes, the early lowering, the drastic lowering, or even extinction of the electroretinogram is a powerful tool. Long before there is a serious increase in night blindness, long before there is any large amount of pigment deposit in retinitis pigmentosa, a change in the electroretinogram often may be found. Here one has from the laboratory a significant aid to clinical diagnosis.

It should be emphasized that there have been recent reports of a few cases which were exceptions to this rule. How well documented these cases are is still open to question.

Certainly, if an extinct electroretinogram is found in an individual suspected of retinitis pigmentosa, it is highly suggestive. One should add that there are a number of experimental eye diseases that can be produced in the laboratory with drugs which were intended for one purpose or another and misfired. For example, iodate which was tried 75 years ago for treatment of puerperal sepsis and was known as "septijod." There is NP207, which I mentioned before, originally introduced as a tranquillizer. There are some new trypanocidal drugs which are diamino-diphenoxy alkanes, each of which seem to affect the retina in a somewhat different manner. By elaborating studies already begun on experimental animals treated with these drugs, it is hoped to learn more about diseases which affect the layer of the pigment epithelium and the retinal receptor cells.

DR. KESTENBAUM: I would like to ask whether in your experience every case of retinitis pigmentosa has disturbance of the electroretinogram from six months of age when normally the electroretinogram becomes observable.

DR. POTTS: We have had very little opportunity to measure electroretinograms in young children. This requires general anesthesia and is a much more formidable procedure than measurements in an individual who can co-operate. This field, therefore, is not yet thoroughly explored. This much is known: in young adulthood when the onset of retinitis pigmentosa is generally recognized the extinguished electroretinogram is a very early, perhaps the first, finding.

What are some simple color vision tests for office practice?

DR. LINKSZ: This is a hard question to answer. What color vision tests are practical depends on what kind of a practice one has and what one is expected to do in that practice. In certain branches of the Armed Forces or in the textile industry the requirements for color vision will be high. For the recognition of traffic signals the requirements are entirely different and, in fact, as Dr. Adler mentioned, good color vision is not at all important for driving a car.

Almost all of us will have the Ishihara plates or some other set of pseudo-isochromatic chart in the office. Such a chart is certainly practical; it also is a very easy test. But how much information does it give? The Ishihara plates or the American Optical Company plates are almost too good. Some eight percent of the male population will, by the use of Ishihara or other pseudoisochromatic test, turn out to have a color vision defect but that test will not give any diagnostic hint about the severity of the defect. The Ishihara test is practical as far as telling that a person is color normal, but it is absolutely impractical as far as telling how severe the color defect of a defective actually is.

Many persons who do not pass the Ishihara or American Optical pseudoisochromatic test might very well qualify on the lantern test. This type of test is used by maritime mustering or employment agencies in many countries. It is much more practical. Usually filtered red, green, and amber lights are shown under all kinds of conditions, simulating fog, rain, and so forth, at all kinds of visual angles, attempting to meet more practical situations. A lantern might not be a practical test for the office because who wants to be bothered running such tests in a busy practice. But no flight surgeon or Navy medical officer can afford to be unfamiliar with it.

The superior diagnostic instrument, the anomaloscope also is not practical for the office. If I were asked what tests to recommend for the office, I would not recommend an Ishihara book or similar pseudo-isochromatic chart. They are for the most rigid requirements.

Of the test charts available in this country one of the best is the HRR (for Hardy, Rand, Rittler) published by the American Optical Company. With this test one can make a rather secure diagnosis in a few minutes. My present favorite is the "Farnsworth 16 hue test." Using this the patient has to put small chips of color into order. This can be done in a minute. The mistakes the patient makes (if he makes any) arrange themselves in certain patterns and one can make a quick diagnosis whether the defect is protanopia, deuteranopia, or tritanopia. In short, there is no one most practical test. For office purposes I think the Hardy, Rand, Rittler and the Farnsworth tests are sufficient.

DR. POTTS: I would like to add a nonlaboratory note of a situation in which the pseudo-isochromatic test is not too delicate. This is the clinical situation of the ever-growing host of electronics people who have occasion to sort out as many as 25 differently colored coded cables which look alike as far as the gray scale is concerned; the differences among the colors are fairly subtle on occasion. These people also have to judge condensors and resistors by a similar pastel-type color tone. These people are in real difficulty. They might well pass a lantern test but would be shown up by a pseudo-isochromatic test.

DR. LINKSZ: The pseudo-isochromatic test is certainly the most delicate and the hardest to pass. If the requirements are very high, I agree that it is the best test.

DR. KESTENBAUM: I have observed that, if a red glass is put in front of one eye, and in front of the other eye a green glass, the patient is immediately able to differentiate between red and green because, when the light breaks down, the red is white for the eye with the red glass and green is white

for the eye with the green glass. This test immediately makes it possible for the color blind man to recognize whether a color is red or green. He can even read the Ishihara test very easily. However, in all my experience the patients were always enthusiastic until I wanted to prescribe for them; then they would say "we don't have to see whether something is red or green."

What is the practical significance of the study of optokinetic nystagmus in a patient?

DR. KESTENBAUM:

1. If homonymous hemianopia is due to a lesion of the middle or the hindmost part of the optic radiation, it is always associated with disturbance of the optokinetic nystagmus on the side of the hemianopia (in rotation of the drum to the opposite side). If the lesion is in any other part of the optic pathway, such as in the optic tract, the anterior part of the optic radiation, or in the visual cortex, the optokinetic nystagmus is not disturbed. Disturbance may mean either decrease or absence of the nystagmus or absence of the quick phase alone so that the eyes follow the fixated stripe but do not return to the original position. One must be careful to rely only on definite differences between the two sides and to ignore small dubious differences. This sign was based on a study of 48 well-localized cases, a reliability of 90 percent, and has just been confirmed by observations of Cogan and his co-workers in Boston.

2. Optokinetic nystagmus serves in the differentiation between the stationary fixation nystagmus from infancy and the later acquired vestibular nystagmus, which signifies the presence of an active disease. In the first case, the optokinetic nystagmus is either absent or substituted by nystagmus-like movements in the opposite direction, a so-called "inversion" of the optokinetic nystagmus. In the second case, the optokinetic nystagmus emerges in a normal way and in only added algebraically to the spontaneous nystagmus.

3. Measurement of visual acuity with the optokinetic nystagmus (Ohm, Goldmann).

4. Testing for central vision in infants over four months of age (already discussed).

Note that optokinetic nystagmus can be suppressed voluntarily, or in disturbed attention, but in this case the optokinetic nystagmus is absent to both sides.

What new diagnostic instruments now in the developmental stage are likely to become significant in clinical practice?

DR. POTTS: In this connection there are the image-amplifying and image-converting devices which are gradually becoming available and which are also gradually being applied to ophthalmology. One of these image-converting devices is the infrared image converter, now going through a rapid series of developmental stages, which converts an image in infrared unseeable by the ophthalmoscopist into a visible picture of certain details in the fundus. If one illuminates the fundus with infrared and uses an image-converter instead of the human eye to see the picture, one can see things which are ordinarily not visible. Even at medium infrared wavelengths, absorption of hemoglobin is much less significant than it is under ordinary visual wavelengths, and the relatively small amount of retinal pigment is transparent. Thus one may certainly look through the retina. Under certain circumstances one may also look through the choroid (and see nothing). Under other circumstances, such as in cases of heavily pigmented tumors of the choroid, there is every reason to believe from early exploratory work that the tumors may be seen behind an otherwise obscuring retinal detachment. Consequently, the image-converter can be of exceptional diagnostic use. It is also conceivable that, in experimental animals at least, injection of dye which is opaque to infrared may allow a careful study of retinal plus choroidal circulation, even in animals whose retinal pigmentation is ordinarily quite heavy.

One step removed from this is the use of television ophthalmoscopy which is more than a fancy gimmick. It allows the whole picture of the retina to be displayed on the television screen, and a single line of the television image can be treated electronically. Thus, if one uses a series of monochromatic lights for illumination, the amount of light reflected back from a lesion in the retina will vary with the wavelengths and, if one can measure this accurately enough, it will give a so-called reflection spectrum of the lesion. With the aid of this type of instrument one can hope to add other specific items to the diagnostic armamentarium for lesions which up until now have not been easily seen. One might add that the great intensities of illumination which are needed for observation of the fundus in monochromatic light (the thing that really makes the red-free filters on ophthalmoscopes impractical) is not a restraining factor with these very sensitive electronic devices. As they become more sensitive the light level needed becomes less and less.

Mention should be made in this connection of the increasingly better known techniques of electromyography for learning about extraocular muscles, and the still not completely common place electroretinography as laboratory instruments which are still being developed but may become clinical tools in the near future.

Dr. Linksz: Thank you. I wish I were 25 years younger so I could live long enough to see how ophthalmoscopy and everything will change. We are very grateful to the members of the Panel for their discussions.

Alan H. Barnert,
Corresponding Secretary.

Ophthalmic Miniature

Koeppe has invented a method which allows an examination of the fundus of the eye with a high magnification by focal light. . . . An identical method allows the examination of the angle of the anterior chamber. The apparatus is very complicated and costly. . . . A maximal dilatation of the pupil is necessary for the examination of the fundus of the eye; for gonioscopy, an instillation of eserine. . . . However meritorious the ingenuity of these researches, it is anticipated that these methods will never be used in current practice.

Koby, F. E.: *Slit-lamp Microscopy of the Living Eye,* 1925, p. 21.

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

EDITORIAL STAFF

DERRICK VAIL, *Editor-in-Chief*
700 North Michigan Avenue, Chicago 11

FRANCIS HEED ADLER, *Consulting Editor*
313 South 17th Street, Philadelphia 3

ALAN C. WOODS, *Consulting Editor*
Johns Hopkins Hospital, Baltimore 5

BERNARD BECKER
640 South Kingshighway, Saint Louis 10

WILLIAM L. BENEDICT
15 Second Street, S.W., Rochester, Minnesota

FREDERICK C. CORDES
384 Post Street, San Francisco 8

SIR STEWART DUKE-ELDER
63 Harley Street, London, W.1

EDWIN B. DUNPHY
243 Charles Street, Boston 14

F. HERBERT HAESSLER
561 North 15th Street, Milwaukee 3

PARKER HEATH
Sullivan Harbor, Maine

S. RODMAN IRVINE
9730 Wilshire Boulevard,
Beverly Hills, California

BERTHA A. KLIEN
950 East 59th Street, Chicago 37

JAMES E. LEBENSOHN
4010 West Madison Street, Chicago 24

DONALD J. LYLE
411 Oak Street, Cincinnati 19

WILLIAM A. MANN
251 East Chicago Avenue, Chicago 11

A. EDWARD MAUMENEE
Johns Hopkins Hospital, Baltimore 5

P. ROBB MCDONALD
Lankenau Medical Building, Philadelphia 31

FRANK W. NEWELL
950 East 59th Street, Chicago 37

JOHN V. V. NICHOLLS
1414 Drummond Street, Montreal

ALGERNON B. REESE
73 East 71st Street, New York 21

PHILLIPS THYGESON
220 Meridian Road
San Jose 26, California

KATHERINE FERGUSON CHALKLEY, *Manuscript Editor*
Lake Geneva, Wisconsin

Directors: WILLIAM L. BENEDICT, President; FREDERICK C. CORDES, Vice-President; WILLIAM A. MANN, Secretary and Treasurer; ALGERNON B. REESE, DERRICK VAIL, ALAN C. WOODS.

Address original papers, other scientific communications including correspondence, also books for review to *Dr. Derrick Vail, 700 North Michigan Avenue, Chicago 11, Illinois;* Society Proceedings to *Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Manuscripts should be *original copies,* typed in *double space,* with wide margins.

Exchange copies of the medical journals should be sent to *Dr. F. Herbert Haessler, 561 North 15th Street, Milwaukee 3, Wisconsin.*

Subscriptions, application for single copies, notices of changes of address, and communications with reference to advertising should be addressed to the *Manager of Subscriptions and Advertising, 664 North Michigan Avenue, Chicago 11, Illinois.* Copy of advertisements must be sent to the manager by the 10th of the month preceding its appearance.

Change of address notice should be received not later than the 10th of the month prior to the issue for which the change is to go into effect. Both old and new addresses should be given.

Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Fifty reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, George Banta Company, Inc., Curtis Reed Plaza, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

ASIA-PACIFIC ACADEMY OF OPHTHALMOLOGY

The First Congress of the Asia-Pacific Academy of Ophthalmology was held in Manila, Philippines, from October 10 to 13, 1960. It was attended by 105 visiting delegates from 12 countries and five continents.

Immediately preceding the Congress, an imposing wreath-laying ceremony was held at the monument of Dr. José P. Rizal, Filipino national hero, humanitarian, scientist, and ophthalmologist.

Following the invocation, delegates were welcomed by the Hon. Felixberto M. Serrano, Secretary of Foreign Affairs, Republic of the Philippines. Secretary Serrano, announced that this was the first international ophthalmologic congress to be held on Asian

soil. He noted that in addition to the great humanitarian and scientific achievement of such a congress, it also signifies a "resurgence and desire of people in neighboring countries to understand related problems, to know one another and to break through political, economic, and other barriers that divided them in the past!"

The principal subject for discussion was "Blinding diseases in Asia."

Speaking from a nutritional standpoint, Dr. D. S. McLaren of the East African Institute of Medical Research, discussed the wide distribution of keratomalacia in Asia and Africa. He emphasized that it was an ocular manifestation of generalized malnutrition. Dr. McLaren also implicated malnutrition as a possible causative factor of high degrees of ametropia in the fetus. Among primary school children living in famine areas of Africa and India, he had found cuneiform opacities in the periphery of the lens. European children raised in the same areas, were free of these lens opacities.

Dr. Oey Khoen Lian further emphasized the prevalence of xerophthalmia as a blinding disease in Indonesia. From Central Java, in 1959, he reported 7,845 children so affected. This figure was higher than those reported during the previous two years.

Dr. J. Bruce Hamilton of Tasmania spoke on the rising incidence of diabetic blindness in Australia.

"Congenital and hereditary blindness in Japan" was the title of a paper given by Dr. Akira Nakajima of Juntendo University, Tokyo. According to Dr. Nakajima, with the control of infectious diseases and the prevention of nutritional deficiencies in Japan, congenital anomalies were becoming increasingly important causes of blindness. In a scholarly and erudite presentation, he alluded to the role of biochemistry as a means of understanding and ultimately controlling genetic abnormalities.

"The surgery of cataract" was presented by Drs. Joaquin Moner Barraquer of Barcelona, Dr. Renald Ching of Hong Kong, and Dr. Sorab N. Cooper of Bombay.

Dr. Geminiano de Ocampo of Manila was the main speaker on a symposium on "Keratoplasty." He discussed basic physiologic concepts and the choice of operation for corneal transplantation.

A full morning was devoted to glaucoma. Dr. Saul Sugar of Detroit was the principal speaker. In addition, seven free papers from as many countries rounded out this symposium.

Papers on strabismus were given by Dr. George Guibor of Chicago and Patricia M. Lance, orthoptist, of Sydney, Australia.

Other papers of special regional interest to ophthalmologists practicing in Asia were those concerning "Harada's disease" by Dr. S. Okamune of Kochi, Japan, "Fungus keratitis" by Dr. S. T. Puttanna of Mysore, India, "Marfan's syndrome" by John Chang of Hong Kong and K. Prommindaroj of Bangkok, Thailand, and "Intraocular cysticercosis" by P. Siva Reddy of Hyderabad, India.

New contributions with vast potentialities were those concerning trachoma. Participating in this symposium were Dr. Hidehisa Fujiyama of Hokkaido University, Japan, on "Culture of trachoma virus on chorioallantoic membrane of developing chick embryo and electro-microscopic study thereof"; Drs. Robert J. Woolridge, J. Thomas Grayston and San Pin Wang of the United States Naval Medical Research Unit No. 2, of Taipeh, Taiwan, on "Immunologic studies on trachoma and experimental trachoma in human volunteers." Dr. Phillips Thygeson of the University of California Medical Center was the moderator. Dr. Thygeson also presented a paper on the "Classification of follicular conjunctivitis."

Dr. Jesus Tamesis, Quezon City, Philippines, spoke on the "Surgical treatment of macular degeneration." He described his technique and reviewed a 12 to 18 months' follow-up of suprachoroidal implantation of the inferior oblique muscle. He observed improvements of the central vision and visual

fields in patients with retinitis pigmentosa, chorioretinal degeneration, high myopia with scleral staphylomatous changes, traumatic and nonspecific chorioretinal degeneration.

"An experiment in social ophthalmology" was the title of an inspiring message by Dr. Ranald Ching of Hong Kong. Dr. Ching spoke of 16 blind boys and girls in the Hong Kong Music Training Center for the Blind. Prior to admission these children were destitute and unwanted. Since admission, each of them had learned to sing, play the piano and another musical instrument. They had given over 200 concerts. Many of them wrote and sang their own compositions. They had also developed a sense of dignity, self-confidence, improved morale and changed outlook on life. Dr. Ching hoped that institutions for the blind in other parts of the world might become interested in sponsoring similar educational programs.

The social part of the Congress was almost as full as the scientific. Dr. Geminiano de Ocampo, president of the Asia-Pacific Academy of Ophthalmology, and Mrs. de Ocampo, entertained members and their wives at a lavish reception; Dr. Jesus Tamesis, executive chairman of the Congress, at a formal luncheon. The First Lady of the Philippines, Mrs. Leonila D. Garcia, invited members to a tea at Malacanang Reception Hall. A formal dinner with a lavish floor show was held on the last day of the Congress. Here old and modern folk and ritual dances and a spectacular floor show featuring Miss Philippines, 1960, were the highlights.

The true spirit of the meeting was reflected in an editorial that appeared in the October 10, 1960, issue of the *Manila Times*.

> This is one of the most important meetings to be held in this country. For here are practitioners, researchers, editors of international fame in their chosen field of ophthalmology. The impressive roster includes delegates from Australia, China, East Africa, Hong Kong, Indonesia, Japan, Korea, Spain, the Philippines, Thailand and the United States—reading in alphabetical order. No apartheid, no segregation, no particular seating arrangement based on differences of religion, political beliefs, or ethnic origin.
>
> Politicians often call scientists naive, gifted but gullible, men who are content to work in their ivory towers insulated by their own talents from the cares and struggles of the common man. Maybe so, but scientists also seem to have stumbled upon a form of brotherhood of men that seems to work. Who knows? Maybe the politicians will use it as a model some day.

William John Holmes.

CONGRESS OF THE JAPANESE OPHTHALMOLOGICAL SOCIETY

The 64th Congress of the Japanese Ophthalmological Society held at Nagasaki, Japan, provided an opportunity to visit Japan in April, 1960. The invitation to be the guest of honor was only the beginning of a long series of gracious attentions that were repeated in many Japanese cities from Nagasaki to Tokyo. Plans for travel, accommodations and entertainment in Japan were made well in advance by Dr. Jun Tsutsui who acted for the society in arranging the itinerary, contact with professors of ophthalmology in 11 medical colleges, banquets and sight-seeing during the three-week visit. So complete were the plans that we were constantly attended and provided with an interpreter from the moment we arrived at the Hanada Airport in Tokyo until we left there three weeks later. Even when we traveled alone by train or otherwise, the attendant knew in advance where we were going and who would meet us. In spite of this close attention we never felt that our privacy was restricted nor that we were directed more than was necessary.

One wishes that all the experiences could be recorded for in such an intimate association many fascinating and often fantastic things occur. When we live closely with the people of an entirely foreign culture we assume many of their patterns; since, during this visit most of our living and eating was in Japanese style, we soon adapted and accepted the use of chopsticks, sleeping on mats in the Japanese style and leaving one's shoes at the door, but our western anatomy did not easily convert to the custom of sitting on the floor.

The Congress under the presidency of Dr. Hirose, professor of ophthalmology, Nagasaki University, was held in Nagasaki where as requested I discussed my research in "Radiation cataract." Approximately 250 ophthalmologists attended the three-day meeting. Since the discussions were in Japanese I did not usually attend but we noted that the meetings were enthusiastically attended and that papers were freely discussed. My paper was given in English, utilizing diagrams which were simultaneously presented in English and Japanese script and there was free discussion of the paper by various members of the society. There was no evidence that the use of English by me presented any problem to the audience.

We visited the Atom Bomb Casualty Commission installations in Nagasaki and Hiroshima where records are maintained on all those in the areas who have survived the bombs. There was opportunity to see outpatients with cataract as well as other patients hospitalized for general disease resulting wholly or in part from atom bomb injury. The Atom Bomb Museums in Nagasaki and Hiroshima, which contain records and artefacts from the destruction of the cities, are grim reminders of the overwhelming devastation of the cities and great suffering of the people. The museums are visited daily by busloads of school children, Japanese adults and foreign visitors who, it is hoped, will be inspired to carry the message of peace to their homeland. This powerful propaganda is handled without sensationalism yet presents its story without restrait. There is no evidence of any motive except to record the history of the effect of the atom bomb.

The Departments of Ophthalmology in the medical schools in Nagasaki, Hiroshima, Tokashima, Okayama, Osaka, Kyoto, Takatsuki and Tokyo were included in our itinerary. There are 47 medical schools in Japan; we visited 11 and in each we were graciously received and entertained by the professor and his staff. Many of the universities and medical colleges are government supported, either on a national or prefectural (regional) basis; however, some very fine private medical colleges, such as Nippon in Tokyo, are outstanding. The medical profession has great prestige and the people look up on the doctors as being very wealthy. The fee for cataract extraction is approximately one-tenth that common in the United States but is three times more than 10 years ago, and is set by the government because of the quite general socialized medicine through employment groups (Communication Hospitals, Postal Workers Hospital, Factory Workers Hospital). Some private practice exists in private—often family—hospitals.

Japanese ophthalmology is ambitious, active and progressive. The staffs of the departments conduct active programs in teaching, research and clinical ophthalmology. Clinical work is done in the morning, while the afternoon, often extending to midnight, is devoted to research. All staff, resident and volunteers take part in the research program. Projects quite similar to those done in this country are being studied but it appeared that biochemistry, virology, visual physiology, aqueous mechanics and electron microscopy were particularly active areas. Reprints of publications were freely given by all departments. Clinical management was similar to that in the United States in most areas. Alpha chymotrypsin was used routinely; corneal heterografts are being investigated; retinal detachments are usually treated by diathermy and scleral resection without plastic implants. Surgery is done in the afternoons —each staff member having one day each week.

It is very difficult to evaluate the clinical facilities because our standards are much different from the Japanese. However, they are progressing and are growing. Nine of the 11 medical schools were building new hospitals or new clinics. The other two had new buildings which were very modern. This does not necessarily mean that they were operated in the American style, yet they were buildings that were of excellent design and well equipped in a manner that we would be proud to have for our own use.

The electron microscope appears to be standard equipment. Operating rooms in new areas were well designed and had much modern equipment. Clinical and research areas had good modern equipment some of which was purchased from the National Council to Combat Blindness grants.

The hospital and medical buildings of Nippon University in Tokyo were particularly impressive for the buildings were new, well maintained and well equipped. The staff at Nippon is exceedingly alert and undertaking a program that is really exemplary and comparable with that in the leading class medical colleges of the United States. Osaka Medical College at Takatsuki has a very fine modern hospital. Other areas must complete their building before they can compete, but in all the colleges visited there was evidence of great ambition and diligence on the part of the professor and staff and of co-operation from the government that will make Japanese ophthalmology a dynamic force in the clinic and laboratory. More and more will their studies be published in English so that more universal dissemination will be possible.

All our time was not spent in laboratories and clinics. We were guests at dinners, geisha parties, Japanese theatres and in the homes of Japanese. We visited temples and shrines, sightseeing in Nara, Hakone, Nikko, Atami, the Inland Sea, and that fascinating Island of Miyajima. The beauty of the country is not exaggerated. The mountains or the sea are always in view and the cherry blossoms cover the land in April.

Beauty, kindness and hospitality are remembered attributes of Japan.

P. J. Leinfelder.

CORRESPONDENCE

Editor,

American Journal of Ophthalmology:

The following communication is on the clinical study on herpes simplex which is a continuation of the work reported on page 42 of this issue. We believe we have a sufficient number of cases for a preliminary report at this time and would like it to be published as a letter.

Treatment of herpetic keratitis by cauterization with silver nitrate

At the present time ether and iodine are accepted chemical cauterizing agents in the treatment of dendritic herpetic keratitis. In our publication on page 42, evaluating the effectiveness of various chemical compounds possessing antiviral activity, the silver ion in the form of silver nitrate was found to inactivate totally the virus in vitro at a concentration of less than 2.0 μg./ml. This degree of potency far exceeded that of numerous compounds, including ether and iodine, and, because silver had little or no toxicity to the cornea at a concentration of 0.5 percent or less, it was selected as a cauterizing agent for human viral infection of the cornea.

To date 20 cases of herpes simplex infection of the cornea at various stages of the disease have been treated by cauterization of the epithelium using 0.5 or 0.25-percent silver nitrate in sterile distilled water. The method is as follows:

The cornea is stained with sterile fluorescein strips, sterile 0.5-percent tetracaine anesthesia is applied topically in drop form, a cotton applicator stick is wetted in 0.5-percent silver nitrate solution (0.25 percent was used in six of these cases) and all infected epithelium is rubbed off. If multiple dendritic ulcers are present over the whole cornea, then de-epithelization of all nonadherent tissue is accomplished even if it involves most of the surface. Cautery is not advised in cases in which ulceration has involved the stroma. Contact of the cornea with 0.25-percent silver nitrate solution may be as long as five to 10 minutes. The eye is irrigated with sterile water or boric acid, one-percent atropine is instilled and the eye is firmly patched and observed daily until re-epithelization has occurred.

The 20 patients treated in this preliminary

study had typical epithelial lesions of superficial herpes simplex keratitis. Other than this, they were a heterogeneous group differing in age, extent, and duration of infection, history, previous treatment, and so forth. They were all treated as described and all recovered in three days with clear corneas. In only two instances was it necessary to repeat the process because of the occurrence on the third day of a small satellite dendritic figure. One of these was treated locally a third time to remove a punctate dendritic mark.

This report can make no true comparison between silver nitrate and other forms of chemical cautery, due to the lack of a sufficient number of patients that could be treated under controlled conditions. However, it may be claimed that patients with dendritic keratitis may be cauterized with silver nitrate in low concentration with no harmful effects. Furthermore, from the standpoint of minimal chemical ocular inflammation, relief of ocular distress and photophobia, patients receiving silver treatment were improved. No instances exhibiting untoward reactions or complications occurred in the patients studied.

It is important to point out that the rationale for using silver nitrate, as for other chemical agents, does not depend upon any special ability for the agent to attack virus in its intracellular habitat. For that matter no compound, including silver nitrate, has yet been found to possess such a property. It is simply an advantage to use a strong virus-inactivating compound during cautery in order to neutralize quickly the infectivity of living virus that is liberated from damaged cells during cauterization and thereby minimize infectivity. This type of therapy has not been tried in cases of deep keratitis with stromal involvement. In such cases there is some possibility of trapping silver deep in the interstitial tissue in the form of insoluble silver chloride or as the reduced free metal. But our experience in treating superficial dendritic keratitis has shown that 0.25–0.5-percent silver nitrate is a mild, nontoxic form of chemical cautery. It is interesting that an agent as old as silver nitrate, used in ophthalmic practice for decades, should be found to have such a potent antiviral activity when compared with over 150 other compounds.*

(Signed) Theodore W. Sery
Philadelphia, Pennsylvania.

* See: Sery, T. W., and Furgiuele, F. P.: "The inactivation of herpes simplex virus by chemical agents," on page 42 of this issue.

Correction

Editor,

American Journal of Ophthalmology:

With reference to my article "Chymotrypsin in dendritic ulcer" published in The Journal (**50**:496 [Sept.] 1960), the concentration was given as 100,000 units dissolved in 5.0 cc. This should read 2,500 units dissolved in 5.0 cc. In other words 500 units per cc. These are Armour units only.

(Signed) Wendell L. Hughes,
Hempstead, New York.

References omitted

Editor,

American Journal of Ophthalmology:

The following references were omitted from my paper, "Head pain" published in The Journal (**50**:654 [Oct.] 1960).

Hamby, W. B.: Intracranial Aneurysms. Springfield, Illinois, Charles C Thomas, 1952.

Poppen, J. L., and Fager, C.: Intracranial aneurysms: Results of surgical treatment. J. Neurosurgery, **27**:283-297, 1960.

Material cited under the sections entitled "Etiology" and "Treatment" should be accredited to them.

(Signed) Hugh C. Donahue,
Boston, Massachusetts.

BOOK REVIEWS

ANATOMY: A REGIONAL STUDY OF HUMAN STRUCTURE. By E. Gardner, D. J. Gray and R. O'Rahilly. Illustrated by C. Henselmann. Philadelphia, W. B. Saunders Company, 1960. 999 pages, profusely illustrated with excellent line drawings in black and white, 65 plates, glossary of eponymous terms, index. Price: $15.00.

This book has had "rave" reviews in general medical journals. It must be agreed that these are justified. After a perusal of this textbook of anatomy, one elderly ophthalmologist wishes that he could renew his youth and undertake once more the gentle joys and sorrows of the dissecting table.

Chapter 71 concerns the orbit and Chapter 72, the eye. These are written by Ronan O'Rahilly, M.Sc., M.D., of Wayne State University, who has done an amazingly good job, with evidence of deep scholarship and wide reading in up-to-date ophthalmic literature, to which reference is freely made. It is extraordinary how accurately and well the author has condensed the gross anatomy into 33 pages. It is hoped that the medical student will not be encouraged to skip these chapters and will come to realize how utterly fascinating the eye can be.

Derrick Vail.

EYE SIGNS IN GENERAL DISEASE. By F. Herbert Haessler, M.D., Professor of Ophthalmology Emeritus, Marquette University. Springfield, Illinois, Charles C Thomas, 1960. 113 pages and index. Price: $5.75.

Intended for the internist or general practitioner, this small book fulfills its purpose through a unique presentation of various eyes signs as related to general diagnosis. It is of some interest to the ophthalmologist because of the eye signs in some of the rarer syndromes, which most of us have difficulty in remembering because of their complicated hyphenations, such as the Block-Sulzberger syndrome, in which a variety of ocular findings have been described.

The general method followed is to present *The Sign* in the form of a concise statement of the findings and changes noted in the eyes, followed by a short paragraph describing *Its Significance*. The introductory section of the book consists primarily of general advice as to methods of examining the eyes, both externally and internally, emphasizing the fact that "you will discover more abnormalities if you have in mind to look for them than if you merely expose your eyes to the field in the hope that the abnormality will obtrude itself upon your consciousness. Inspection must be an active process not a passive one."

Simplicity of presentation and terminology will make this book one which the general physician can peruse without undue effort or expenditure of excessive time. An extensive diagnostic armamentarium is not required although it is assumed that an ophthalmoscope is available. Study of this book will certainly convince him that knowledge of many eye signs will assist him in making a diagnosis. No attempt is made to discuss therapy or to go into great detail. In many instances references are included for those who wish more complete information. In no sense supplanting such standard works as those of Sorsby or Tassman, this volume presents succinct information in an original and simplified manner. Illustrations have been kept at a minimum.

William A. Mann.

TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM: Volume LXXIX, Session 1959. London, J. and A. Churchill, Ltd. 770 pages and index. Price: not listed.

This is the 79th volume of the *Transactions* of the Ophthalmologic Society of the United Kingdom and continues the standards of literacy and good humor which have characterized the preceding volumes. Of particular interest is a symposium of ocular injuries and

surgery of the eyelids. It is gratifying to note that the techniques first devised by our own John Martin Wheeler are now universally accepted. A most interesting paper is that of Brig. J. D. Welch on the organization of ophthalmic out-patient departments. He makes many excellent suggestions on the organization of such a department but I think that most of us would take issue with his advice to leave refractions to opticians. Certainly in teaching institutions it is necessary and wise that the resident staff and attending men interest themselves in the problems of refraction rather than delegate this to an optician.

The Doyne lecture this year was by Dr. L. Paufique on the treatment of retinal detachments. He reviews the history of treatment of retinal detachments and evaluates them. He is definitely in favor of prophylactic diathermy of the superior quadrants in patients undergoing cataract extraction, if there is a history of detachment in the other eye or high myopia. This is certainly not the general practice in the United States and deserves to be investigated more thoroughly here.

The most amusing and stimulating article in the *Transactions* is that by Trevor-Roper on "The ontogeny and phylogeny of visual artistry." A beautifully organized discussion begins with the blue "paintings" of Bowerbirds and proceeds through the daubs of the anthropoid apes and continues on to the art work of very small children and older children with reduced vision. Attempts at representational painting in this latter group results in two dimensional pictures much like those of the early Assyrians and Egyptians. Dr. Trevor-Roper concludes that two- or three-dimensional representationalism is a highly developed artistic response and has taken thousands of years to achieve. With great restraint he refrains from commenting on the abstract and nonobjective art of today. This one article is well worth purchase price of the entire volume.

The second major section of the *Transactions* is devoted to the Oxford Ophthalmological Congress held in 1959. An unusual feature of this meeting is the section devoted to the after-thoughts of previous Doyne medalists. Also worthy of mention are articles by Spaeth on cataract surgery on the myopic eye, and particularly a paper by H. B. Stallard on the treatment of malignant melanomas of the choroid with radioactive applicators. By and large this treatment is reserved for patients whose only eye is involved by a malignant process. However, Dr. Stallard's good results make one wonder whether his treatment might not also be used as a substitute for the routine mutilating enucleation whose value is always in doubt in these cases. A provocative and invaluable paper.

David Shoch.

Industrial Arts for Blind Students. New York, American Foundation for the Blind, 1960. 80 pages, paperbound. Price: $1.00.

Education in industrial arts is "the doing phase" of education. Such education for the blind includes among many objectives the inculcation of an active interest in industrial life, a mastery of orientation and mobility skills, knowledge of tools and machines, appreciation of good design and workmanship and resourcefulness in meeting practical situations. As the materials used are all drawn from industry, the training provides a good foundation for later vocational education. This booklet aims to promote the development of standards in this field. It was designed primarily as agenda for the 1960 first summer session of industrial arts instructors of blind students, a project financed by the federal government.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

François, J., Verriest, G. De Rouck, A. and Rabaey, M. **Comparative study of the retinal histology and electroretinogram in batrachians and reptiles.** Ann. d'ocul. **193**:752-767, Sept., 1960.

This is the third and concluding part of a three-part article, the first two of which appeared in the preceding numbers. Since this section is quite technical what follows is the authors' summary. The authors have compared the histological and electroretinographic features of specimens from 34 species, which represent most of the important families of amphibians and reptilians. The sensory layers were studied, using a classification of the photoreceptors in which both the phylogenetical homologies and the functional analogies are taken into consideration; the ratios between the numbers of nuclei in the different layers of the retinas were also systematically studied. White stimulations of varying exposure-times and frequencies were used during the electroretinographic examination; the influence of the adaptation-state was also taken into account.

The ratios between the cellular richness of the different retinal layers can be correlated to the form of the electroretinogram, to the duration of the stimulus/relative amplitude of the d-wave-curve and to the frequency of stimulation/relative amplitude of the answer-curve. The duplication of some components of the electroretinogram is not necessarily due to a duplex character of the sensory layer. The specimens belonging to the salamandrids, discoglossids, pelobatids, bufonids, hylids and crocodilids may be considered as typically nocturnal. The specimens belonging to the agamids, iguanids and lacertids are typically diurnal. Between these two groups, with extremely opposite characters, were found pipids, ranids and turtles and also some anguids, chamaeleontids and colubrids, which appeared to be less diurnal than the majority of the lacertilians.

This work includes also an extensive survey of the literature based upon the morphologic and functional data relating to the retinas of the amphibians and of the reptilians. (5 figures, 2 tables, 127 references) David Shoch.

Okamoto, Tamae. **A study on the gen-**

esis of the spiral nerve ending in the extrinsic ocular muscle. Jap. J. Ophth. **4**: 12-15, Jan.-March, 1960.

The author found that the spiral nerve ending, which is believed to be the sensory nerve ending in the extraocular muscles in man, begins to develop just before birth. The fact that the motor nerve ending develops earlier in the extraocular muscle than the sensory spiral nerve ending suggests that the correlation of monocular and binocular movements which are integrated for binocular single vision develops some time after birth. (8 figures, 16 references) F. H. Haessler.

Omoto, Sumio. **The histological investigation on the nerves of the extrinsic ocular muscles of the rabbit.** Jap. J. Ophth. **4**:152-162, July-Sept., 1960.

The third, fourth and sixth cranial nerves at the exit from the brain contain 4827, 867, and 1413 nerve fibers, respectively. Each trunk has five percent more fibers in the distal than in the proximal part. Communications with the frontal and trochlear nerves were noted in the orbit and in the cavernous sinus. No communications between the third and sixth nerve and ophthalmic division were found in either the orbit or the cavernous sinus.

The innervation ratio for the superior oblique muscle of the rabbit was 5.6, that is, 886 nerve fibers supplied 4997 muscle fibers. (34 figures, 4 tables, 21 references) Author's summary abbreviated.

Ribas Bensusan, Jose. **Intraocular factors in accommodation.** Arch. Soc. oftal. hispano-am. **19**:977-982, Dec., 1959.

A detailed description of the anatomy and physiology of the ciliary muscle and lens is given. (2 figures) Ray K. Daily.

Sorsby, A., Stone, J., Leary, G. A. and Sheridan, M. **Changes in the depth of the anterior chamber and in the radius of curvature of the front surface of the lens during growth. Observations on the rabbit.** Brit. J. Ophth. **44**:467-471, Aug., 1960.

The depth of the anterior chamber increases by 0.6 mm. up to 20 weeks and then remains relatively stationary. The anterior surface of the lens continues to flatten between 60 and 80 weeks. The greatest lenticular change occurs in the first 12 weeks. (1 table, 2 figures, 6 references) Irwin E. Gaynon.

2
GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Jawetz, E., Thygeson, P., Hanna, L., Dawson, C. and Mitsui, Y. **"Trachoma viruses" isolated in the United States,** J. Cl. Invest. **39**:1000-1001, June, 1960.

A brief abstract is presented of a paper read before the May 2, 1960, meeting of the American Society for Clinical Investigation. The authors claim to "have succeeded in growing for the first time 'trachoma viruses' from patients in the United States." Two such viruses are described, one of which, after serial transfer in embryonated eggs, produced a typical, acute trachoma in human volunteers, but was not infectious for "small, laboratory animals" or tissue cultures. The other, isolated from a man who had acquired the disease twenty years before in Pakistan, and who had been symptomless for five years, produced in monkeys a minimal follicular reaction and rare inclusions. It is suggested that persistence of the infection, or geographic origin, may influence the pathogenic properties of the virus. Lawrence T. Post.

Mérte, Hans-Jürgen. **Experimental study of the spirochetal antigen and antibody reactions in the cornea.** Arch. f. Ophth. **162**:279-285, 1960.

Experimental studies of the pathogenesis of parenchymatous keratitis were made on the cornea of rabbits which had been infected with syphilis three months to three years before by the injection of spirochetes into the testes. Spirochetal antigen was injected into the corneal lamellae and there was an immediate anaphylactic reaction. One may conclude that antibodies against spirochetal antigens were present. The results of these experiments support the view of Igersheimer that luetic antibodies are present in the cornea of persons with congenital lues. (2 figures, 7 references)

F. H. Haessler.

Perret, D. and Mann, I. **Isolation of virus from embryonate eggs inoculated with material from a case of trachoma in western Australia.** Brit. J. Ophth. **44**:503-505, Aug., 1960.

The psittacosis-lymphogranuloma venereum group of viruses was isolated from embryonate eggs inoculated with conjunctival scrapings taken from a clinical case of trachoma in an Australian aboriginal boy. (2 tables, 4 references)

Irwin E. Gaynon.

Verdi, G. P. and Serra, C. **Isolation and cultivation of the herpes simplex virus from human ulcerative keratitis.** Boll. d'ocul. **38**:705-730, Sept., 1959.

The authors isolated the virus of herpes simplex from 30 patients with dendritic keratitis. They attempted to culture the virus using human amniotic fluid, rabbit kidneys, human embryos, monkey heart, and monkey kidney. The most sensitive culture media proved to be human embryos and rabbit's kidney. (9 figures, 3 tables, 78 references)

Joseph E. Alfano.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Alagna, G. **The effect of tioctico acid on the toxicity of ditizone.** Arch. di ottal. **64**:75-86, March-April, 1960.

Ditizone in rabbits will elevate the blood sugar and within a few days cause cataract and chorioretinitis. Tioctico acid is an amino acid present in the protein of mammals, which like glutathione, cysteine, and methionine, has the sulfhydril radical.

Rabbits were given intravenous ditizone 80 mg./Kg. Those which also received intramuscular tioctico acid showed a lower blood, aqueous and vitreous glucose concentration on the sixth, eighth and sixteenth day. There was definite protection against cataract and retinal change. The possible mechanism is discussed, and many possible physiological functions of tioctico acid are described. (1 table, 36 references) Paul W. Miles.

Clement, F. **Stability of the vitreous gel. A new technique for measuring it.** Arch. Soc. oftal hispano-am. **19**:948-964, Dec., 1959.

This is a report of an experimental study on cows' eyes. The vitreous was cut into eight to 16 pieces, and the volume of each fraction was measured before and after heating it. The fluid of the vitreous was drained off by filter paper, and the vitreous gel placed in tightly closed tubes. The tubes were submerged for two minutes in warm water of determined temperature and the heating process arrested by cooling the tubes for three minutes in running water. The thermic retraction of the vitreous of the cow shows individual variations and variations due to age. The integrity of the hyaloid does not influence the thermic stability of the vitreous. It is shown that the effect of the pH is the opposite of that found in colagen and

other proteins. A marked increase in the thermic retraction of the vitreous was associated with pH values distant from that of the isoelectric point. With a pH under 5 and over 9.5 the retraction is practically total. The effect on the thermic stability of vitreous of various salts in various concentrations was also studied. A marked diminution in the thermic stability of the vitreous is created by its deprivation of hyalouronic acid. Alcohol and acetone had no influence. Formic aldehyde diminishes greatly the thermic retraction of the normal vitreous as well as that of vitreous previously modified in its pH. (8 figures, 2 tables) Ray K. Daily.

Cloud T. M., Hakim, R. and Griffin, A. C. **Photosensitization of the eye with methoxsalen.** A.M.A. Arch. Ophth. **64**: 346-351, Sept., 1960.

Exposure of white guinea pigs to long-wavelength ultraviolet light after the intraperitoneal injection of methoxsalen can result in serious ocular complications. Black guinea pigs were much less severely affected. There is also evidence that long-term use of this drug can produce cataract in laboratory animals when there is a short daily exposure to ultraviolet light. Since this drug is used in this country not only for therapeutic reasons but also for sun-tanning, caution is indicated until the possible eye complications are studied in man. (1 figure, 19 references) Edward U. Murphy.

De Berardinis, E. **Determination of cytochrome C and of the cytochrom oxydase activity in the bovine retina.** Acta ophth. **38**:448-451, 1960.

Cytochrome C occurs in the bovine retina in a concentration of about two micrograms per gram of tissue. Cytochromoxydase is present and its activity can be expressed as reduction of the logarithm of the molar concentration of cytochrome C reduced by a solution of the tissue 1:100 in one minute, its mean value being 0.36. (3 references) John J. Stern.

Evans, C. D., Herxheimer, A. and Lee, B. E. **A method for assessing the stinging sensation caused by eyedrops.** Ophthalmologica **139**:431-438, May, 1960.

The principle of the method is to instill two different solutions simultaneously in the two eyes of the individual who is to describe the stinging sensation in quantitative terms. The test individual as well as the examiner are not informed of the composition of the solutions which are used. In every case one solution was saline while the other was 2-percent amethocaine (tetracaine) in one of three vehicles, namely—a boric acid buffer, a phosphate buffer or the vehicle of the British National Formulary (methylhydroxybenzoate 0.023-percent and propyl hydrohybenzoate 0.011-percent in distilled water). All solutions were brought to body temperature before instillation. There was no significant difference between the subjective stinging sensations elicited by the three solutions. The authors conclude that at least as far as amethocaine is concerned there is no advantage in using buffered vehicles. Comparisons of the pharmacologic effects of the three solutions were apparently not made. (7 tables, 5 references) Peter C. Kronfeld.

François, J., Rabaey, M. and Recoules, N. **The free amino acids in the aqueous and interstitial corneal fluid of cattle.** Ophthalmologica **139**:424-430, May, 1960.

By two-dimensional paper-chromatography the free amino acids in the fluids stated in the title were individually identified and their approximate concentrations estimated before and after deproteinization. The interstitial fluid of the cornea of cattle eyes is characterized by a high glutamic acid and the aqueous by

a high methionine content. (5 figures, 8 references) Peter C. Kronfeld.

Lijo Pavia, J. and Marcone, G. **Physiology of the human macula.** Rev. otoneuro-oftal. Sudam. **35**:1-14, Jan.-May, 1960.

The authors describe extensively the anatomy and physiological characteristics of the human macula. Walter Mayer.

Propst, A. and Hofmann, A. **Electronmicroscopic study of the zonular fibers, particularly the effect of trypsin.** Arch. f. Ophth. **162**:269-278, 1960.

Details, of enzymatic zonulolysis are described and it is made clear that the "enzymatic zonulolysis" in cataract extraction cannot be ascribed entirely to the action of the ferment. (4 figures, 13 references) F. H. Haessler.

Quaranta, C. A. and Vozza, R. **Histologic studies of the choroid and retina following the administration of Ditizone and sodium iodoacetate.** Boll. d'ocul. **38**:665-683, Sept., 1959.

The authors studied the histologic appearance of retinas in rabbits after the systemic administration of Ditizone and sodium acetate.

Ditizone produced a diffuse chorioretinitis with optic atrophy and retinal gliosis. The iodoacetate had a more selective action on the visual cells and the pigmentary epithelium of the retina with a secondary atrophy of the overlying retina. No change in the choroid or optic nerve was noted after the administration of iodoacetate. (14 figures, 11 references) Joseph E. Alfano.

Sekiguchi, Kunio. **Histological studies on the ocular toxicity of α-chymotrypsin.** Jap. J. Ophth. **4**:104-116, April-June, 1960.

In a study of the possible untoward effects of α-chymotrypsin on the ocular tissues, 0.002, 0.02, and 2 mg. of the drug in 0.1 cc. of physiologic saline solution were injected into the vitreous and 0.02 and 0.2 mg. were injected into the anterior chamber of white rabbits. The reaction of the eye to these injections was noted in histologic studies. Injection of α-chymotrypsin into the vitreous body, even in the low dosage of 0.02 mg., caused more or less severe changes in all the ocular tissues, of which the damage to the retina was particularly serious. It was noteworthy that the cornea was little affected in any case, despite such prominent lesions in the other ocular tissues. When introduced into the anterior chamber, even 0.2 mg. of the drug caused no perceptible damage to the ocular tissues. (24 figures, 5 references) F. H. Haessler.

Vozza, R. and Negroni, G. **Action of Cycloserine, Pyrazinamide and Vyomicin on experimental ocular tuberculosis in the rabbit.** Boll. d'ocul. **38**:817-832, Nov.,1959.

The authors studied the action of Cycloserine, Pyrazinamide and Vyomicin on experimental ocular tuberculosis (immuno-allergic, ocular infection) in rabbits. They found that Pyrazinamide and Cycloserine were ineffective in preventing the ocular reaction whereas Vyomicin was found to be extremely effective. However, upon the cessation of Vyomicin therapy the ocular inflammation not only recurred but seemed to be more violent. (1 figure, 2 tables, 37 references) Joseph E. Alfano.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Dreyer, V. **Visual contrast thresholds. IV. The influence of the background area on thresholds, determined by the method of variable stimuli.** Acta ophth. **38**:470-484, 1960.

The study comprises an investigation of the contrast thresholds for various

small visual angles, examined in the course of step-wise variation of the area of the background by means of dark framing. The contrast thresholds are determined by the method of varying stimuli, found for both positive and negative stimuli. Two threshold criteria are used: the just imperceptible stimulus and the just perceptible stimulus. The background luminance is varied in three steps, the highest being approximately 100 cd/sq.m.

The experimental results lead to the following conclusions: 1. For all background areas, a graphic presentation of the threshold values for positive stimuli follows a curve pattern which is similar to experiments with infinite background. The dependence of the thresholds on the stimulus visual angle is characterized by a critical visual angle. Above this value of angle, the contrast demand is independent of the stimulus visual angle, while below it, the demand increases progressively with decreasing visual angle. 2. With moderate background luminances, a framing of the field has the result of lowering the threshold for positive stimuli seen under large visual angles. In such cases, the stimulus is experienced as being brighter than the background, even though its luminance can be measured as being less than that of the background. 3. For negative stimuli seen under small visual angles, the curve changes its shape completely, when the background area is reduced by framing. When the stimulus visual angle becomes less than a critical minimum value, stimuli which continue to be perceived as darker than the background, are measured as having luminances which increasingly exceed the beckground luminance. Hereby, thresholds for negative stimuli approach thresholds for positive stimuli. 4. For the just imperceptible negative stimulus, the demand for contrast is independent of the visual angle of stimulus, when the background luminance is sufficiently great. Quite analogous conditions can be found with an infinite background. However, framing has the effect that the stimulus is experienced as being darker than the background, even when the stimulus luminance is measured as being greater than the background luminance. This latter peculiarity also holds for thresholds for the just perceptible stimulus, at large background luminance. 5. The paradoxical situations in which the subjective brightness of the stimulus deviates from its objectively measured luminance, can be explained on the basis of the phenomenon of simultaneous contrast. 6. The experiments appear to confirm that there is not merely a quantitative difference, but also a qualitative difference, between the perception of positive and negative stimuli. (3 tables, 8 figures, 13 references) Author's summary.

Erikson, A. S. **A case of unilateral transitory myopia in association with catarrhal fever.** Acta ophth. **38**:437-441, 1960.

A 16-year-old girl showed a change of refraction in one eye from +0.5D to −6.5D during a general, influenza-like infection. The unaffected eye had a +3.0D hypermetropia with a congenital coloboma of iris, choroid and retina. The depth of the anterior chamber of the affected eye had increased by over 0.5 mm. Edema of conjunctiva and fundus were observed and edema of the ciliary body assumed, which would explain the change of refraction. Allergy to the infective process is supposed to be responsible for the condition. (1 figure, 7 references)

John J. Stern.

François, J., Verriest, G. and De Rouck, A. **New electroretinographic findings obtained in congenital forms of dyschromatopsia.** Brit. J. Ophth. **44**:430-435, July, 1960.

Frequent investigations have set an acceptable standard for waves of the electroretinograph; variations in these tracings have been reported in cases of achromatopsia. The authors report the results of a study of dark-adapted and light-adapted eyes by means of a neon stroboscope in patients with dyschromatopsia. The results obtained in deuteranomalous, deuteranopic, and tritanomalous subjects were identical to those found in normal eyes, whereas the tracings made in protanomaly, protanopia and typical achromatopsia showed a single b-wave which differed from the normal. This difference was considered to be significant. (4 figures, 30 references) Morris Kaplan.

Lima, F. **Studies on post-images.** Rev. brasil. oftal. **19**:177-184, Sept., 1960.

The author reviews our present-day knowledge of post-images and their application to the newer methods of pleoptics, which he discusses extensively.

Walter Mayer.

Oksala, A. and Lehtinen, A. **Light transmission of the corneal epithelium examined with an emission spectrograph.** Acta ophth. **38**:371-376, 1960.

The light transmission of bovine corneal epithelium was examined with Hilger's emission spectrograph, using an iron arc. The lower transmission threshold lies at 2831 Angström units; a steep rise brings it to 65 percent at 3100 A, where a slow increase occurs up to 4300 A. (69 percent). Between 4300 and 5200 A another abrupt increase occurs to 95 percent. (3 figures, 4 references)

John J. Stern.

Toki, Tatsuo. **Treatment of myopia with local use of neosynephrine hydrochloride.** Jap. J. Ophth. **4**:213-219, July-Sept., 1960.

Local application of 5-percent solution of neosynephrine hydrochloride at home before sleeping is a very simple method of treatment of myopia and yields no ill side effects. The results were most satisfactory, so that even four to five months after the completion of the treatment increase of naked eye vision by 0.23 and a decrease of the refractive degree by 0.14 diopters in average respectively could be attained when compared to those at the first examination. This method should be recommended for the treatment or prevention of the progress of myopia. (4 figures, 1 table, 9 references) (Published in J. Clin. Ophth. 14:248, 1960 in Japanese.)

Author's summary.

Van Assen, E. C. **The role of electroretinography in the diagnosis of total color blindness.** Ophthalmologica **139**:494-496, June, 1960.

The diagnosis of congenital color blindness by the usual means (pseudo-isochromatic plates, anomaloscope) becomes uncertain in cases with superimposed, degenerative or inflammatory, macular lesions. In the three adult siblings of a Dutch family the presence of degenerative macular lesions injected such an element of uncertainty into the diagnosis of congenital color blindness which was suggested by the results of the usual color test, the horizontal nystagmus, and the reduced central visual acuity. Electroretinography clarified the situation by demonstrating markedly reduced responses of large retinal areas under photopic conditions. (3 figures, 3 references) Peter C. Kronfeld.

Wybar, K. and Thatcher, B. **Significance of eccentric fixation in squint.** Brit. J. Ophth. **44**:472-491, Aug. 1960.

Visual function is developed in the macula by the sixth year of life. Both foveas are associated in the visual process. The receptors in the macula are concerned with high visual acuity. The retinal receptors have a spatial sense.

Suppression is initiated in the cerebral cortex.

Amblyopia occurring at birth (arrest) is more dense than that occurring later (extinction). Eccentric fixation is concerned with the alteration in the spatial sense of the retinal receptors of the squinting eye. Abnormal retinal correspondence is a binocular phenomenon. The correspondence is a binocular phenomenon. The correspondence of the squinting eye is not centered in the macula. Occlusion of the squinting eye merely accentuates abnormal retinal correspondence. It would be better to occlude the deviating eye.

The visuscope is used to establish extrafoveal fixation, which may be constant or it may have several points of fixation. The visuscope is also useful in determining the state of binocular correspondence.

The euthyscope (after-image production from fovea) provides useful information in eccentric fixation in diagnosis and prognosis. The ability to convert a positive after-image into a negative one is a favorable sign.

The coordination makes use of Haidinger's brushes, which can only be seen if there is some macular function present.

The euthyscope is used to restore normal spatial values in the macula. After the spatial relationship has been restored the problem of improving central visual acuity is approached by utilizing the negative phase of the after-image test.

The coordination is used where the eccentric point lies within three degrees of the fovea or where the euthyscope has developed some macular function. (9 figures, 7 references) Irwin E. Gaynon.

5

DIAGNOSIS AND THERAPY

De Ruyter, J. **Cybernetic disturbances as the cause of a fairly frequent complex of ophthalmological symptoms.** Ophthalmologica **139**:469-475, June, 1960.

A 26-year-old student of ethnology working on his thesis had two principal types of complaints, 1. inability to adjust promptly to a change in illumination and 2. persistent whirling sensations after brief exposures to lively patterns of quickly moving or quickly changing objects. Complaints of this type are fairly common in the author's practice. "These patients are entirely normal and well-balanced aside from their inability to digest agitating observations." This inability is attributed to a disorder in the feedback mechanism in the central nervous system. This disorder is comparable and analogous to a disturbance in an electric brain which, due to a fault in the machine, keeps on repeating the same answer to a single question. Peter C. Kronfeld.

Djordjevic, L. and Stojanovic, D. **Implantation of placenta into the anterior chamber: therapeutic results in various eye diseases.** Ophthalmologica **139**:453-461, June, 1960.

A piece of preserved placenta 7 mm. long, 2 to 3 mm. wide and 0.5 mm. thick is introduced into the anterior chamber through a small corneo-scleral incision under a limbus-based flap. This is done in such a way that about half of the implant stays in the chamber and the other half in the subconjunctival space. The method was used in this series of 64 patients representing a great variety of inflammatory and degenerative ocular diseases. The implanation caused a mild anterior segment reaction in the course of which the implant itself was absorbed. Clinical improvements are reported. (1 figure, 1 table, 38 references)

Peter C. Kronfeld.

Fankhauser, F. and Schmidt, T. **The optimal conditions for studies of spatial summation by quantitative light-sense perimetry with stationary targets.** Ophthalmologica **139**:409-423, May, 1960.

The authors have continued Gold-

mann's and their own previously reported studies in basic quantitative perimetry. They have added to the original Goldmann perimeter a device for movement of the targets at accurately controllable speeds and an arrangement for static perimetry.

The present paper concerns itself with three basic aspects of perimetry: 1. the effect of the method of testing, static or kinetic, on the differential threshold of a given retinal area, 2. the effect of different states of adaptation on the differential threshold and on the degree of spatial summation, and 3. the effect of background brightness, area tested, and target size upon the scatter and experimental error in measurements of differential thresholds and spatial summation.

The most definite finding was that the degree of spatial summation increases with decreasing background brightness. The scatter of summation or differential threshold measurements is so great that only marked deviations from the means determined by the authors may be interpreted as being pathologic. (16 figures, 7 references) Peter C. Kronfeld.

Freudenberg, K., Meyerratken, E. and Pablitzsch, H. **A comparison of the results of objective measurements of visual acuity with the instruments of Goldmann and of Günther.** Arch. f. Ophth. **162**:318-338, 1960.

The authors examined 263 patients with both instruments, 479 with the instrument of Goldmann, and 763 with that of Günther. In all of the patients aggravation was suspected. The data were analyzed statistically. With a visual acuity between 0.01 and 0.25 the method of Günther is clearly superior and the probability that this finding is not accidental is 100 percent; for visual acuity between 0.30 and 1.25 there is no significant difference between the two methods. (10 tables, 27 references) F. H. Haessler.

Galdino, M. **Recent advances in ocular anesthesia.** Rev. brasil. oftal. **19**:241-248, Sept., 1960.

The author describes the pharmacology of the different substances used for preoperative medication. He then describes the various drugs used for local anesthesia for a Van Lint and a retrobulbar blocking. He describes also his technique for intravenous use of Demerol in hypertonic glucose solution, 50 mg. in 100 cc. (8 references) Walter Mayer.

Tengroth, B. **A new model of the Lindner stenopic glasses.** Acta ophth. **38**:442-443, 1960.

An improved model is described in which the pupillary distance can be adjusted by means of a friction joint at the juncture of the right and left half, and peripheral vision is excluded by foam plastic tubes attached to the back surface of the frame which can be cut to fit the contour of the face and can be removed and cleaned. (2 figures) John J. Stern.

Yamamori, Akira. **New electronic ophthalmodynamometer.** Jap. J. Ophth. **4**:175-185, July-Sept., 1960.

The author describes a new electric ophthalmodynamometer. Since the intraocular pressure is recorded continuously throughout the procedure there is no need for recording the so-called initial pressure nor a calibration line. The measurements are easily made, the results are recorded with exactitude, and there is no room for interjected subjective impressions of the examiner. (6 figures, 6 references) (Published in Acta Ophth. Jap. 64:417, 1960 in Japanese.) F. H. Haessler.

6

OCULAR MOTILITY

Arruga, A. and Downey, R. **Anomalous sensory relationship in apparently cured squints.** Brit. J. Ophth. **44**:492-502, Aug. 1960.

During the past few years it has been found, by the use of pleoptic methods, that many patients who are presumed to have normal binocular single vision after optical, orthoptic, or surgical treatment, still do have a small angle of anomaly. There is restricted amplitude of fusion and true stereopsis is absent.

Occlusion with full optical correction should be continued in children until the child is old enough to undertake exercises and is ready for surgery. (6 figures, 8 references) Irwin E. Gaynon.

Dal Fiume, E. and Cardi, G. **Clinical study of acute strabismus due to occlusion.** Arch. di ottal. **64**:87-108, March-April, 1960.

A review of the literature revealed only 12 cases of heterotropia excited by ocular occlusion. Occlusion strabismus has been described in older children and young adults as a latent tropia made manifest by an injury or disease requiring an eye bandage. It has also followed psychic trauma. Four cases presented by the authors were very interesting. An 18-year-old patient had keratoconjunctivitis from ammonia. After bandaging the eye for 20 days there was esotropia which required four months of orthoptics for relief. At the end, the eyes were orthophoric at distance and esophoric at near.

In a child aged seven years an eyelid abscess was bandaged for three days. This was followed by esotropia and diplopia which required eight months of orthoptic treatment. The third case was similar and the fourth occurred in an 8-year-old child who was occluded for amblyopia ex anopsia and esotropia developed. When the occlusion was stopped, the esotropia disappeared. (2 figures, 15 references) Paul W. Miles.

Matteucci, P. and Pasino, L. **The value of stability and eccentricity of monocular fixation in the amblyope with strabismus.** Ann. d'ocul. **193**:733-738, Sept., 1960.

All amblyopes with strabismus may be divided into two groups. Group 1 consists of those cases, usually in children, in which there is unstable fixation. In this group fixation is usually foveal but the children are unable to maintain this fixation and there is poor hand-eye coordination. A second group, smaller in number, consists of those patients, usually older, who have eccentric fixation in which there is good hand-eye coordination, but this coordination is always off just a little bit because of eccentric fixation. Obviously, the former responds much more easily to occlusion and orthoptics. The second group is that which requires foveal stimulation and pleoptic treatment. (1 figure, 15 references) David Shoch.

Ugawa, Tokunosuke. **Divergence excess.** Jap. J. Ophth. **4**:185-190, July-Sept., 1960.

The study of a patient with divergence excess suggested that an exophoria which becomes manifest with distant vision is the result of an anomaly of postural tonus and passive divergence which is the result of elasticity of the orbital structures. The position of the eyeballs approaches that of orthophoria in near vision because the outward deviation is overcome by excellent proximal convergence. (3 figures, 1 table, 14 references) (Published in Acta Ophth. Jap. 63:4311, 1959 in Japanese.) F. H. Haessler.

7

CONJUNCTIVA, CORNEA, SCLERA

Almeida, J. **Surgery of pterygium.** Rev. brasil. oftal. **19**:253-256, Sept., 1960.

The author describes in detail his technique of removing pterygium. He feels strongly that the cornea must be cleaned completely of any remnants whatsoever of the pterygium and of the entire conjunctiva and subconjunctiva connected with the pterygium. He extends his dis-

section to the caruncle and down to the rectus muscle. If this technique is followed recurrences will be held to a minimum. (3 references) Walter Mayer.

De Gastro, J. **Rare corneal injury due to spine of echinoderm.** Rev. brasil. oftal. **19**:249-252, Sept., 1960.

The author presents the case of a boy who accidentally was struck in one eye by an echinoderm, a sea star. The patient had minimal pericorneal flush, and slight lacrimation. Slitlamp examination revealed numerous corneal and intracorneal foreign bodies. Some of these foreign bodies were removed but the deeper ones were left in place. After a few days all the deeper seated foreign bodies had come to the surface and either dislodged themselves from the cornea or could be removed easily with a spatula. (2 figures, 5 references) Walter Mayer.

Forgacs, J. **Clinical and experimental study of the basal membrane of the corneal epithelium in keratitis bullosa.** Brit. J. Ophth. **44**:385-393, July, 1960.

The existence of a basal structure between the corneal epithelium and Bowman's membrane has been frequently described and its histopathology has been well studied. This membrane is independent of the tissues on either side of it but it seems to have an adhesive role between the two. To demonstrate this role, experimental keratitis bullosa was caused in rabbits' eyes by replacing the aqueous with a 10-percent solution of sodium chloride and then placing the eye in distilled water; in another series the eyes were placed in a solution of trypsin. In the first group there were few and small bullae while in the second group the number and size of the bullae were appreciably increased which indicates that the enzyme interfered with this adhesive action. In several clinical cases of dystrophy it could be demonstrated that there were alterations in the structure of this basal membrane. (8 figures, 25 references)

Morris Kaplan.

Geeraets, W. J., Chan, G., and Guerry, D. **Corneal antigenicity.** A.M.A. Arch. Ophth. **64**:413-425, Sept., 1960.

The individual corneal layers of the rabbit eye were tested separately for their antigenicity and ability to participate in specific antigen-antibody reactions. Immuno-electrophoresis and agar diffusion were the techniques used. Fifteen different responses were found, some related to the different structures and others nonspecific. (9 figures, 16 references)

Edward U. Murphy.

Hirano, Junzo. **Histochemical studies on the corneal changes induced by corneal contact lenses.** Jap. J. Ophth. **3**:1-8, Jan.-March, 1959.

Histochemical changes of the rabbit cornea when a corneal contact lens was applied to it were investigated. The most remarkable changes were recognized in the distribution of glycogen in the corneal epithelium. Slight decrease in epithelial glycogen could be seen three hours after the insertion and complete disappearance after 24 hours. In the limbal region, however, it remained normal 24 hours after the insertion.

RNA and amino acid in the protoplasm of the epithelial cells decreased gradually after the disappearance of glycogen, but DNA in the nucleus was always intact.

Histologically the disarrangement of epithelial cells and the slight thickening of the corneal stroma were observed after 24 hours, and desquamation of epithelium, opacity and thickening of the stroma was evident after 48 hours. These changes were especially marked in the central region of the cornea.

The recovery process of the cornea was observed after previous insertion of the

corneal contact lens for 12 hours. The resynthesis of epithelial glycogen has been seen after three hours and it was completed after 12 hours. No effect of habitual wearing for five weeks was observed histologically.

The injury of the cornea by the insertion of the corneal contact lens was recognized as far slighter than that which followed the wearing of the scleralcorneal type. (19 figures, 11 references) (Published in J. C. Ophthalm. 12:431, 1958 in Japanese.) Author's summary.

Hofmann, H. and Propst, A. **Experimental study of corneal injury by α chymotrypsin and trypsin.** Arch. f. Ophth. **162**:225-268, 1960.

The action of these zonulolytic ferments on the injured cornea of rabbits was studied at intervals of 15 minutes to six days by means of biomicroscopy and also in histologic preparation. Descemet's membrane was found to be very resistent but the layers of collagen fibers became swollen after exposure to the ferment for 60 minutes and completely dissolved in 48 hours. Details of this process are described. The injured cornea is more severely injured by α chymotrypsin than by trypsin. (13 figures, 12 references)

F. H. Haessler.

Kamiya, S., Horiuchi, T., Hatakeyama, A., Abe, K. and Matumura, T. **Transplantation of the parotid duct into the conjunctival sac for the treatment of xerophthalmia.** Jap. J. Ophth. **3**:189-196, July-Sept., 1959.

The authors confirmed the feasibility of the transplantation of the parotid duct into the conjunctival sac by experimental work on the dog and the human cadaver. The parotid duct has been successfully transplanted into the conjunctival sac in fifteen dogs. The procedure was applied clinically in seven cases of xerophthalmia which occurred after trachoma. The prognosis of these patients was observed postoperatively for two and a half to 13 months. Treatment was successful in four cases and unsatisfactory in three cases as a result of stoppage of secretion, formation of cyst, and excessive secretion. (3 figures, 1 table, 9 references) (Published J. Clinic. Ophthalm. 13:295, 1959 in Japanese.) Authors' summary.

Kaufman, H. E. **The diagnosis of corneal herpes simplex infection by fluorescent antibody staining.** A.M.A. Arch. Ophth. **64**:382-384, Sept., 1960.

Fluorescein-labeled herpes simplex antibody was used on corneal scrapings from 17 eyes and a diagnosis could be made rapidly. (4 figures, 7 references)

Edward U. Murphy.

Mills, N. L. and Donn, A. **Incorporation of tritium-labeled thymidine by rabbit corneal endothelium.** A.M.A. Arch. Ophth. **64**:443-446, Sept., 1960.

Evidence of mitosis was found in rabbit corneas by this method after endothelial abrasion. (4 figures, 10 references)

Edward U. Murphy.

Mitsui, Y., Kurihara, H. and Ohtsubo, M. **Punctate superficial keratitis after topical prednisolone.** Ophthalmologica **139**:461-467, June, 1960.

In seven patients with anterior uveitis treated topically with prednisolone, the authors observed the development of a punctate superficial keratitis, usually confined to the central or lower central area of the cornea. The keratitis came on after several weeks of prednisolone therapy and subsided after a few weeks, irrespective of whether the steroid was continued or stopped. The authors assume activation of a benign local fungus. (2 figures, 5 references) Peter C. Kronfeld.

Röe, O. **Problems of penetrating corneal grafting. Late results in 18 cases.** Acta ophth. **38**:377-393, 1960.

The union of graft and cornea is not sufficient before three weeks after operation. Local cortisone treatment inhibits the invasion of new vessels into cornea and graft; it should, however, not be used until three weeks have elapsed because wound healing may be interfered with. To facilitate careful control of cortisone administration the patient should stay in hospital for six to eight weeks. Beta rays may cause complications such as delayed wound healing or cataract; they should be used only if very strong indications exist. The problem of the quality of the donor cornea is reviewed. (16 figures, 47 references) John J. Stern.

8
UVEA, SYMPATHETIC DISEASE, AQUEOUS

Barishak, Y. R. **In vitro behaviour of the pigmented cells of the retina and uvea of the adult human eye.** Acta ophth. **38**: 339-346, 1960.

In tissue cultures only the non-pigmented layer of the ciliary epithelium and the posterior layer of the iris showed mitotic activity and rapid proliferation. The growth of the retinal pigment epithelium and the anterior layer of the iris epithelium was less active; the pigment layer of the cilary epithelium, the uveal melanocytes and the clump cells of the iris showed only migration. No active pigmentogenesis could be demonstrated. (4 figures, 9 references) John J. Stern.

Davidson, Sidney I. **Spontaneous cysts of the ciliary body.** Brit. J. Ophth. **44**:461-466, Aug., 1960.

Two cases of spontaneous cysts of the ciliary body are reported. In one of them the mass arose from the anterior part of the cilary body and in the other from the posterior part of the ciliary body. The etiology, clinical features, and treatment are discussed. (4 figures, 35 references) Irwin E. Gaynon.

Ikui, H., Kimura, K. and Nishio, T. **Further studies on sympathetic ophthalmia with electron microscope.** Jap. J. Ophth. **3**:29-37, Jan.-March, 1959.

Electron microscopic studies in ultrathin sections of the uveal tissues in sympathetic ophthalmia were performed in three cases. The cytoplasm of some epithelioid cells presented various pictures of the formation of melanin pigment occurring in it. The pigment granules in these cells are quite different from those phagocytized by leucocytes and by HeLa cells. These facts, together with the light microscopic findings obtained in the same disease, prove that the epithelioid cells in sympathetic ophthalmia are nothing but metamorphosed chromatophores.

The indubitable and invariable presence of virus-like particles in the matrix region as well as in and around the cytoplasmic inclusion bodies in some epithelioid cells —a fact observed in the eyeballs with sympathetic ophthalmia—has enhanced the possibility that the causal agent of this eye disease may be a chromatotropic virus. (9 figures, 9 references) (Published in Acta Ophth. Jap. 62:276, 1958 in Japanese.) Authors' summary.

Konno, Shin-ichi. **Experimental studies on the action potential of the iris.** Jap. J. Ophth. **4**:194-212, July-Sept., 1960.

Dodt reported on the direct induction of the action current of the iris by stimulation of the cervical sympathetic nerve. In Dodt's case this action current appeared as a slow potential variation similar to the c-wave of the ERG. The present author checked Dodt's investigation, and demonstrated that this potential variation was nothing but an artifact.

Induction by stimulation of the oculomotor nerve ended in failure owing to the appearance of large artifacts.

Light stimulation is best suited for the study of the action potential of the iris. By this means the present author could

record the so-called EPG. But direct induction is practically impossible with this method.

The perfect exclusion of movement artifacts is indispensable for the success in induction, but the extreme difficulty of inserting electrodes into the microscopic muscles of the iris makes the experiment of induction in situ practically impossible. Placing the electrodes on the iris surface leaves much room for the appearance of movement artifacts. Of course, artifacts due to stimulation also disturb potential recording. Stimulation artifacts, however, will be excluded in future by the development of a perfect isolator and a dual beam oscilloscope.

In short, the so-called EPG could be obtained through indirect induction, but failure seems unavoidable at the present level of technical development. (15 figures, 3 tables, 10 references) (Published in Acta Ophth. Jap. 63:3569 and 4485, 1959 in Japanese.) Author's summary.

Marconcini, Eraldo. **Posttraumatic cyst of the iris.** Arch. di Ottal. **64**:109-117, March-April, 1960.

The author describes two cases of posttraumatic cyst of the iris. In one of them the cyst arose rapidly 14 years after simple contusion. F. H. Haessler.

McCarthy, J. L. **Mechlorethamine hydrochloride (nitrogen mustard) treatment of experimental tuberculous uveitis.** A.M.A. Arch. Ophth. **64**:396-407, Sept., 1960.

Anterior tuberculous uveitis was produced in non-tuberculin-sensitive rabbits. Intravenous treatment with nitrogen mustard produced only temporary inhibition of the disease process. (16 figures, 17 references) Edward U. Murphy.

Oksala, A. **The significance of treatment by antibiotics and steroids in acute anterior uveitis.** Acta ophth. **38**:405-409, 1960.

In 310 cases antibiotic therapy did not shorten the duration of the disease. Cortisone therapy significantly shortened the duration of treatment. (2 tables, 16 references) John J. Stern.

Paliaga, G. P. **A biomicroscopic histological study of particulate formations concentrated about the anterior ciliary arteries.** Boll. d'ocul. **38**:867-972, Nov., 1959.

The author reports the presence of small particles resembling droplets having a diameter of 60 to 80 microns which were observed about the anterior ciliary arteries. He believes that these formations have not been previously described. These particles were usually seen in older people with tortuous ciliary arteries; histologic sections revealed that they were of lipoid nature. (2 figures) Joseph E. Alfano.

Zamorani, G. **Contribution to the knowledge of neuro-panuveitis.** Boll. d'ocul. **38**:846-853, Nov., 1959.

The author defines neuro-panuveitis as a panuveitis associated with edema of the retina, edema of the nerve head and, in fifty percent of the cases, retrobulbar neuritis. He presents six cases and suggests that this condition might be considered as an incomplete form of the Vogt-Koyanagi-Harada syndrome. (6 references) Joseph E. Alfano.

9

GLAUCOMA AND OCULAR TENSION

Armaly, M. F. **Schiøtz tonometer calibration and applanation tonometry.** A.M.A. Arch. Ophth. **64**:426-427, Sept., 1960.

The ocular tension of 1,072 eyes was measured both with the electronic tonometer and the Goldmann applanation instrument. The good agreement between mean readings obtained by the two methods is not reflected in the results in in-

dividual eyes. The implications are discussed. (3 figures, 12 references)

Edward U. Murphy.

Campbell, D. A. **Effect of neptazane on intra-ocular pressure in relation to its systemic action and its clinical application.** Brit. J. Ophth. **44**:415-429, July, 1960.

The beneficial effects of diamox in the treatment of both acute and chronic glaucoma are well known; the author describes the results of studies of neptazane, a chemical closely related to diamox. It might well be substituted when diamox fails to benefit or causes unpleasant side-effects. This new drug appears to be as effective as diamox though of somewhat slower and less dramatic action and therefore particularly suitable for long-term therapy. Its ideal dosage is 125 mg. once every 24 hours and there seem to be very few unpleasant side effects.

In a series of clinical tests, five patients were treated with various dosages and tested for the drug's general systemic action as well as its intraocular action. A single dose of 250 mg. gives almost the same results as 250 mg. of diamox but the action is slower and more prolonged. With the lowering of intraocular pressure, there is a fall of sodium, potassium, chlorides, and proteins of the blood with a six to seven-hour delay in reduction of bicarbonate. A moderate diuresis occurred. In repeated doses of 125 mg. every 24 hours there was an overall decline in ocular tension which tended to increase with time while in diamox administration the tension tends to rise with time. After one or two days the urinary output of sodium, potassium, and chlorides declined and the output returned to the initial level. Increased or decreased dosage gave no better control of the glaucoma. Except where immediate action is desired, neptazane is equal to diamox for long-term therapy and is to be preferred in many cases. (10 figures, 11 references)

Morris Kaplan.

Colenbrander, M. E. **Measurement of the excavation.** Ophthalmologica **139**:491-493, June, 1960.

The author presents a graphic method for the recording of the approximate outlines of the glaucomatous excavation. (1 figure)

Peter C. Kronfeld.

Drance, S. M. **Ethoxyzolamide (cardrase) in the management of chronic simple glaucoma.** A.M.A. Arch. Ophth. **64**:433-437, Sept., 1960.

Eighteen patients with glaucoma which was not controlled by miotics were treated with this drug in addition. About half were controlled and 25 percent were not. The rest showed control of intraocular pressure but the drug had to be discontinued because of side effects. (3 tables, 4 references)

Edward U. Murphy.

Giardini, A. and Paliaga, G. P. **Treatment of glaucoma using phospholine iodide.** Boll. d'ocul. **38**:684-693, Sept., 1959.

The authors studied the effect of phospholine iodide in concentrations of 0.125 percent and 0.25 percent in both normal and glaucomatous eyes. In 20 normal eyes the drug induced a marked miosis which persisted as long as 20 days. It also induced a constant lowering of the intraocular pressure varying from 2 to 10 degrees. In 60 glaucomatous eyes (primary and secondary glaucoma) the effect of this drug was compared to the anti-hypertensive effect of pilocarpine and a mixture of pilocarpine, eserine, adrenalin, neosynephrine and diamox therapy. The latter combination was considered intense glaucoma therapy. In these 60 eyes pilocarpine alone controlled the tension in 23.3 percent of the cases, phospholine iodide in 56.6 percent, and the intense miotic and diamox therapy in 71.6 of the cases. Sixty percent of the patients complained of blurring of vision and supraciliary pain after the instillation of phospholine iodide and in five percent of the

cases treatment had to be discontinued because of this. (3 figures, 4 references)

Joseph E. Alfano.

Merté, Hans-Jürgen. **Modification of tonography on the basis of theoretic considerations and clinical observation of the behavior of the intraocular pressure during the examination.** Arch. f. Ophth. **162**:299-317, 1960.

The value and range of error of tonography are extensively and exhaustively analyzed. (5 figures, 7 tables, 7 references)

F. H. Haessler.

Schultz, R. O., Watzke, R. C., and Sawyer, T. R. **The long-term results from cyclodialysis.** A.M.A. Arch. Ophth. **64**: 408-412, Sept., 1960.

60 cases were followed from five to 20 years. In 53 percent the tension was 22 mm. or less. The great majority of failures was evident within three years. In 38 percent of cases where the tension was controlled, the eye showed further visual field loss. The best results from this procedure were seen in the mildest cases and the finding which had the greatest prognostic significance was a glaucoma cup. (2 tables, 13 references)

Edward U. Murphy.

Soeteren, T. **Aqueous flow in hypotonic and glaucomatous eyes.** Acta ophth. **38**: 347-362, 1960.

1. In normal eyes which were hypotonic after compression, there was flow of aqueous humor in the episcleral veins when the intraocular pressure was 7.24 mm. Hg or higher. The pressure in the recipient blood vessels must therefore have been less than 7.24 mm. Hg. This value is much lower than that found by other investigators for venous pressure (measured episclerally) in normal, undisturbed eyes and it is therefore reasonable to assume that the pressure in the recipient blood vessels falls when the intraocular pressure is reduced.

2. In eyes which were hypotonic (intraocular pressure between 4.5 and 8.5 mm. Hg) as a result of disease, aqueous veins were observed, and the pressure in the recipient blood vessels must thus have been lower than the intraocular pressure.

3. After compression of eyes with glaucoma simplex there was still aqueous humor drainage in the episcleral veins and the pressure in the recipient blood vessels must thus have been lower than the intraocular pressure. In spite of the fact that the compression caused a considerable reduction of the intraocular pressure (from 7 to 25 mm. Hg), there was no marked change in the appearance of the aqueous veins. This may indicate that the outflow resistance or the pressure in the recipient blood vessels was reduced after compression. (3 figures, 3 tables, 83 references) (Author's summary)

John J. Stern.

Vannas, S. **Experimental studies on iron compounds in the eye and their significance for the pathogenesis of hemorrhagic glaucoma.** Acta ophth. **38**:461-469, 1960.

Ferric citrate and colloidal iron compounds were injected into the vitreous, the anterior chamber, or intravenously in 46 rabbit eyes and one human eye which was to be enucleated for malignant melanoma. The eyes were enucleated five minutes to one month later. Ferric citrate disappeared quickly and did not seem to be bound by ocular tissues. Colloidal iron carbohydrate complex indicated potential absorption binding and was found in the structures leading out from the eyes, similar to the localization of post-hemorrhagic hemosiderin. Intravitreal iron injection resulted in vitreal binding and diffusion or phagocytosis in a backward direction into the perivascular spaces of retina and optic nerve. It was also found in the ciliary processes and the perichoroidal spaces and the sclera.

Intravitreal injection of iron was fol-

lowed after one to two weeks by hyperemia and hemorrhage in the ciliary processes. The breakdown of these hemorrhages resulted in new iron-containing products. These observations confirm the author's view of the significance of the iron-containing disintegration products for the pathogenesis of hemorrhagic glaucoma. (5 figures, 12 references)

John J. Stern.

Vannas, S. and Tarkkanen, A. **Glaucoma and serum cholesterol.** Acta ophth. **38**:452-460, 1960.

The serum cholesterol was determined in 185 patients with simple glaucoma, 115 with angle-closure glaucoma, and 209 controls. No differences were found in the cholesterol values in simple or angle-closure glaucoma and the controls. There was no significant relationship between serum cholesterol level and age in any group. High cholesterol levels have possibly an indirect contributory role in visual field losses. (5 tables, 31 references) John J. Stern.

Yttebory, J. **The role of intraocular blood volume in rigidity measurements on human eyes.** Acta ophth. **38**:410-436, 1960.

The manometric rigidity coefficient is distinctly higher in enucleated eyes than in living eyes. Continuous recording of pressure in vivo shows rapid changes in each individual tonometry, indicating that blood is expelled from the eye during tonometry; the volume of blood expelled varies greatly from eye to eye and decreases with rise in pressure. Compression of the ipsilateral carotid artery causes reduction in ocular blood volume and a rise in rigidity coefficient values, even at identical pressure levels. These findings explain differences between clinically determined rigidity coefficients and manometrically determined ones in eyes in situ which are subsequently enucleated. The rigidity coefficient of enucleated eyes is considerably higher at body temperature than at room temperature. Tonometer calibrations on enucleated eyes at room temperature, as practiced heretofore, have evened out the difference between the curves for them and those carried out in vivo which would otherwise exist because of the importance of the intraocular blood volume. (7 figures, 8 tables, 48 references) John J. Stern.

Zoldan, T. **Marchesani's syndrome.** Boll. d'ocul. **38**:753-763, Oct., 1959.

The author reports a case of Marchesani's syndrome (congenital ectopia of lens, spherophakia and bradydactyly) associated with chronic simple glaucoma in a 43-year-old white female. He thought the case was of interest because of the rarity of the association of glaucoma in these cases. The glaucoma in the right eye was controlled with iridectomy and that of the left eye by iridencleisis. (5 figures, 19 references) Joseph E. Alfano.

10
CRYSTALLINE LENS

Almeida, J. **Surgery of cataract.** Rev. brasil. oftal. **19**:227-239, Sept., 1960.

The author describes in great detail, his own routine technique for cataract extraction: his sterilization of instruments, the local and general preparation of the patient, preoperative medication and anesthesia of the globe, followed by Chandler's maneuver of ocular compression. He opens the chamber with the point of a von Graefe knife or a Gillette blade, enlarges the incision with scissors, and uses sutures as described by McLean. He uses alphachymotripsine and feels that penicillin solution may tend to inhibit this substance, so that he does not use irrigation with penicillin until after the eye has been irrigated with the enzyme. He also gives a brief summary of

his routine postoperative care. (18 references) Walter Mayer.

Binkhorst, C. D. **Experiences with various types of implants in unilateral aphakia. The pupillary or iris-clip lens.** Ophthalmologica **139**:500-503, June, 1960.

This is an abridged version of an article on the same subject published in Am. J. Ophth. 49:703-710, April, 1960.

Peter C. Kronfeld.

Kennedy, P. J., Jordan, J. S., Morrison, J. F., Mulberger, R. D., and Boland, S. W. **Enzymatic zonulolysis as an aid in cataract surgery.** A.M.A. Arch. Ophth. **64**:342-345, Sept., 1960.

432 cataract extractions using alpha-chymotrypsin were done in four hospitals by 10 surgeons. The early results were uniformly good. There was no difference in the results with catgut or silk sutures. There were only three cases of vitreous loss but eight lenses were dislocated into the vitreous by the extracting instrument. All of these were looped uneventfully. (11 references) Edward U. Murphy.

Menna, F. **Enzymatic zonulolysis for extraction of the crystalline lens. (Experiments in guinea-pigs.)** Arch. di ottal. **64**:119-128, March-April, 1960.

Lenses were removed from the eyes of guinea pigs after zonular irrigation with alpha-chymotrypsin of various concentrations. Half of the group had irrigation to flush out the enzyme before extraction. After seven days the eyes were enucleated and studied histologically. All concentrations used were effective, but the stronger ones did interfere with cicatrization. (10 figures, 11 references) Paul W. Miles.

Pintucci, F. **The Amsler-Huber test and exzymatic zonulolysis in cataract surgery.** Boll. d'ocul. **38**:743-753, Oct., 1959.

The author compared the Amsler-Huber test on a group of patients that had undergone cataract extraction in the usual way, with a group of patients that had undergone cataract extraction by exzymatic zonulolysis. His wished to determine whether the reduced trauma to the ciliary body resulting from enzymatic zonulolysis produced a diminished alteration in the blood-aqueous barrier. The studies showed no difference in the behavior of the blood-aqueous barrier in patients who had been operated upon with zonulolysis and those operated on without zonulolysis. (6 figures, 26 references)

Joseph E. Alfano.

Tupinamba, J., Filho, A. A., Lemos da Silva, J. L. and Malta, A. S. **Recent advances in the surgical therapy of cataracts.** Rev. brasil. oftal. **19**:203-224, Sept., 1960.

This paper is a symposium on techniques of cataract surgery presented by the senior author and his collaborators, in which such subjects as preoperative medication and anesthesia, sutures, iridectomies and iridotomies, lens extraction, and enzymatic zonulolysis are discussed. (39 references) Walter Mayer.

Valk, L. E. M. and Tiddens, H. **A case of retrolental fibroplasia treated and cured with oxygen in alternating concentrations.** Ophthalmologica **139**:475-480, June, 1960.

In a premature infant with a birthweight of 700 gm. the signs of retrolental fibroplasia, that is small hemorrhages, folds of the peripheral retina, vascularization and strand formation in the vitreous, disappeared completely on oxygen administration in concentrations gently undulating between 20 and 30 percent.

Peter C. Kronfeld.

Voisin, J. and Paquelin, A. **Preliminary note on the treatment of senile cataracts by a sulfonamite: II (*p*-amino-benzosulformidophyrimidine)** Ann. d'ocul. **193**:768-770, Sept., 1960.

Since the publication of an article in the German literature in October, 1959 on the medical treatment of cataracts with a sulfonamide drug, much has appeared in the lay literature on this subject. The authors felt that the material should be given a critical trial and they have therefore begun to prescribe this drug for a group of patients with senile cataract. The experiment has not gone on long enough to obtain any data on the value of this material, but the authors have noted many complications. Among these they report eczema, digestive disorders, and a granulocytopenia. They do feel that in some cases there has been a general improvement in the health of their patients and in their psychic state. This may have some effect on the report of improved vision. However, they emphasize that more time must elapse before any definite conclusions can be drawn from their study. David Shoch.

11
RETINA AND VITREOUS

Bauermann, M. **Critical evaluation of electron-optic studies of the vitreous.** Arch. f. Ophth. **162**:244-254, 1960.

The author gives his reasons for believing that the findings of Schwartz with the electronmicroscope confirm the conclusions of Bauermann and Thiessen. (4 figures, 7 references) F. H. Haessler.

Heidensleben, E. **Blood pressure on both arms in relation to occlusion in the retinal vessels.** Acta ophth. **38**:444-447, 1960.

In 20 patients with one-sided occlusion of the retinal vessels it was found that the average blood pressure was higher on the side of occlusion, but the difference from a control group was not statistically significant. Thromboses were nearly always localized in the right eye, (nine out of eleven) embolisms in the left one (six out of nine). (1 table, 11 references)
John J. Stern.

Ikui, H., Nonaka, M., Miyozoki, I. and Yamamoto, I. **Adult ocular toxoplasmosis. Report of a case of central exudative retinitis due to toxoplasmosis.** Jap. J Ophth. **4**:77-82, April-June, 1960.

An adult male patient with central exudative retinitis was examined and the causal agent, Toxoplasma gondii, was found in his cerebrospinal fluid. The parasites were isolated in mice after intraperitoneal inoculation with the cerebrospinal fluid. (2 figures, 10 references) (Published in J. Clinical Ophthalmology 13-1485, 1959 in Japanese.)
Authors' summary.

Keerl, Gerhard. **The readaptation of the retina after photocoagulation.** Arch. f. Ophth. **162**:219-226, 1960.

The author studied the effect of therapeutic photocoagulation of the retina on the dark adaptation of 15 eyes of 14 patients. A variable delayed beginning of adjustment of the rods was found. The return to the normal curve of the individual must occur in at most one or two hours, even though quantities up to 110 million Lux were used. In only three patients was a delayed cone adaptation noted. This reaction can be ascribed to extreme light action only with reservation; other circumstances also are probably responsible. (4 figures, 1 table, 7 references)
Author's summary.

Kobayashi, Fumiko. **Genetic study on retinitis pigmentosa.** Jap. J. Ophth. **4**:82-88, April-June, 1960.

In the course of study on the inheritance of retinitis pigmentosa, the author has found a pedigree in which the trait has been transmitted for three generations as a sex-linked trait which has not yet been recorded in the literature. This mode of inheritance has not been described for this disease, though the existence of such a trait had not yet been denied. By the author's discovery of this pedigree, all

theoretically possible modes of inheritance have been described for retinitis pigmentosa.

Slight fundus change indicating chorioretinal atrophy was found in two females, three years old, in the pedigree, though no subjective complaint had been noticed. This slight change had developed to a typical retinitis pigmentosa when examined two and a half years later. This finding indicates that retinitis pigmentosa begins with a slight chorioretinal atrophy, and such a slight fundus change will serve as a clue to the early diagnosis of the disease. Such an observation is possible only by a pedigree study such as this.

One of the patients in this pedigree showed a fundus change just like retinitis punctata albescens. This finding indicates that some cases of so-called retinitis punctata albescens may be an atypical form of retinitis pigmentosa.

The study of this pedigree shows that there is a group of retinitis pigmentosa which accompanies myopia. It was shown that the myopia accompanying retinitis pigmentosa is not a linkage of two genes but pleiotropic effects of a single gene producing fundus change as well as refractive error. (1 figure, 10 references)

Author's summary.

Manuel, Y., Royer, J., Richard, G. and Creyssel, R. **Electrophoresis of proteins in the sub-retinal fluid in primary detachments of the retina.** Ann. d'ocul. **193**:739-751, Sept., 1960.

Sub-retinal fluid obtained in 34 cases of primary retinal detachment was analyzed by paper electrophoresis, starch gel electrophoresis, and immuno electrophoresis. In every case serum albumin was found in the subretinal fluid. In 29 of the 34 cases a beta-globulin was also found. In 14 of the cases a pre-albumin spot was noticed whose nature is still undetermined. The authors feel that this might be a seromucoid. In seven cases a gamma globulin component was also noted. This confirms previous reports in the literature that the subretinal fluid is derived from the blood plasma. It is analogous to interstitial fluid. There seems to be a higher protein content in the subretinal fluid when there have been several operative procedures. The authors speculate that with repeated surgery the original transudate changes to a type of exudate. (3 figures, 2 references)

David Shoch.

Oksala, A. **The echogram in exudative retinitis (Coats' Disease).** Acta ophth. **38**:364-370, 1960.

The echogram made it possible to exclude simple retinal or choroidal detachment in an eye with absolute glaucoma and a dark tumor mass in the vitreous. The echogram demonstrated heterogenous tissue with either calcium or bone conglomerations (bone tissue was found after enucleation). It was not possible to differentiate between retinoblastoma and exudative retinitis; the latter diagnosis was confirmed histologically. (4 figures, 14 references)

John J. Stern.

Sedan, J. and Farnarier, G. **Results of scleral resection in retinal detachments in the aphake.** Ann. d'ocul. **193**:721-730, Sept., 1960.

The authors report 22 cases of aphakic retinal detachment in which a lamellar scleral resection was performed. Using anatomical reattachment of the retina as a criterion of success, they report a success rate of 59 percent. This series of 22 cases is compared with a similar one of 25 cases previously reported. This original series had only diathermy coagulation as a therapeutic procedure. In the later series the success rate based on the same criterion was 52 percent. The authors therefore feel that scleral resection is a better approach to the treatment of aphakic retinal detachment than simple diathermy coagulation. (48 references)

David Shoch.

Valk, L. E. M., Beaumont, P. and vanderBoogard, J. **Favorable effect of Duraboline on diabetic retinopathy.** Ophthalmologica **139**:480-484, June, 1960.

Duraboline, an androsterone derivative with minimal masculinizing property was used in one case of far advanced diabetic retinopathy. Changes in the eyegrounds that occurred during this treatment are interpreted as favorable effects of the drug. (11 references)

Peter C. Kronfeld.

Zangger, J. and Marx, J. **The possible antibacterial activity of the human vitreous.** Arch. f. Ophth. **162**:237-243, 1960.

Extensive study revealed no antibacterial activity. The well-known fact that the vitreous is a good culture medium for many organisms was confirmed. (4 figures, 15 references) F. H. Haessler.

12

OPTIC NERVE AND CHIASM

Regnetti, E. **The treatment of acute retrobulbar neuritis of unknown etiology.** Boll. d'ocul. **38**:789-801, Oct., 1959.

The author decribes the treatment of 86 cases of retrobulbar neuritis of unknown etiology in his clinic from 1936 to 1958. In the early years the treatment consisted of polyvalent vaccine (Mixogon), sodium salicylate, urotropin, vitamin B and vitamin C. When the antibiotics penicillin and streptomycin came into use it was found that these drugs alone did not have a favorable effect. During the last three years treatment has been replaced by prednisone derivatives in association with transfusion of plasma or human blood. The author stresses particularly the usefulness of human plasma in the treatment of this condition. (3 tables, 42 references)

Joseph E. Alfano.

13

NEURO-OPHTHALMOLOGY

Battistini, A. **Pupillographic studies in a case of homonymous hemianopsia.** Arch. di ottal. **64**:129-134, March-April, 1960.

In an elderly patient with hypertensive vascular disease and homonymous hemianopsia, the author found the Lowenstein method of pupil reflex photography very useful. (3 figures, 6 references)

Paul W. Miles.

Davidson, S. I. **Ocular aspects of electromyography.** Brit. J. Ophth. **44**:394-405, July, 1960.

Electromyography has proven of real diagnostic value to the clinical ophthalmologist and a plea is made for its more general use; its value in studies of the action of the levator palpebrae superioris and of the inferior oblique are especially emphasized. The procedure records the electrical potentials created by the muscle fibers contracting in response to a nerve impulse. These potentials are measured in micro-volts (one millionth of a volt) and are recorded on a drum for interpretation. The procedure has limited application in assessing nerve pathology but has great value in the diagnosis of ocular myopathies such as myasthenia gravis and phorias or tropias due to defects of motility of one or more muscles. (12 figures, 24 references) Morris Kaplan.

Fujino, T. and Go, Y. **On the retinal representation in the lateral geniculate body.** Jap. J. Ophth. **4**:1-7, Jan.-March, 1960.

Retinal representation in the lateral geniculate body was studied experimentally on 16 Macaca cyclopses leading to the following results.

Retinal representation of the crossed and uncrossed fibers in the lateral geniculate body has two theories: Minkowski's specific layer presentation theory and Brouwer and Zeeman's opposing theory.

Findings in Nissl's stain specimen proved the superiority of the former. Diffuse presence of Marchi's granules in the lateral geniculate body after single-eye removal was the reason of opposition to Minkowski's theory but the meaning of this fact was unknown to anyone. The authors have found that the optic fibers run diffusely in the lateral geniculate body from the oral side to the caudal side. This is why the granules were present in the normal cell layers of the lateral geniculate body in Marchi's stain after removal of one eye. This finding made it possible to acept Minkowski's theory without hesitation.

The optic fibers form small bunches in the lateral geniculate body. They are prominent in the oral part of the lateral geniculate body, counting 3,600 in one sample, and decrease in the caudal side, disappearing completely at the caudal pole. This finding is ascribed to gradual termination of small bundles in the lateral geniculate body.

Representation of various areas of the retina in the lateral geniculate body was studied by Marchi's method, and the findings obtained agreed grossly with that of Brouwer and Zeeman. (6 figures, 5 references) Authors' summary.

Jain, N. S. **Familial synkinesis in oculopalpebral movements.** Brit. J. Ophth. **44**:506-507, Aug. 1960.

Two cases of congenital ptosis in sisters are reported. Versions were normal. Elevation was absent or grossly restricted. Looking down caused abduction in one eye. (9 figures)

Irwin E. Gaynon.

Sugawara, Syuji. **Experimental studies on the allergy of the brain with special reference to the mechanism and pathogenesis of retrobulbar neuritis. Report I. Serological and histological studies.** Jap. J. Ophth. **3**:54-68, Jan.-March, 1959.

Aiming at clarifying the pathogenesis, the mechanism, and the actual changes in retrobulbar neuritis due to demyelinating diseases, which represent multiple sclerosis and other undetected causes, serologic and pathologic studies were performed. Using rabbits, the emulsion of heterologous, homologous, or their own brain tissue was injected.

The rabbits fell into palsy of extremities about three weeks after. The paralysis originated in the white matter. In all cases a specific antibody to the brain was produced. It was also specific to the optic nerve. In each group, correlation was proved between the antibody value and the rate of paralysis. The antibody contributes a great deal to produce paralysis because paralysis appears when the antibody value reached the maximum.

The changes in the optic nerve were similar to those of the other parts of the central nervous system. The main change consisted in demyelination with perivascular inflammatory changes. The mechanism may be rationally explained by the theory of brain allergy. (13 figures, 5 tables, 14 references) (Published in Acta Ophthalm. Jap. 62:1506, 1958 in Japanese.) Author's summary.

Thiel, H.-L. **The diagnosis and therapy of arachnoiditis opticochiasmatica.** Arch. f. Ophth. **162**:227-236, 1960.

From the clinical study of five patients the author derives the characteristic symptomatology of arachnoiditis opticochiasmatica. Whereas headache, multiform defects in the visual field and visual acuity, and the exclusion of numerous differential diagnostic entities usually lead to correct diagnosis, the changes in the optic disc are entirely uncharacteristic. The author discusses the etiologic possibilities and therapeutic procedures. (6 figures, 22 references) F. H. Haessler.

Toyama, Tomio. **The retinal blood pressure in choked disc.** Jap. J. Ophth. **3**:216-223, July-Sept., 1959.

In 51 patients with choked disc, caused by brain tumor, the retinal blood pressure was measured by Mikuni's ophthalmodynameter. The results were as follows:

The retinal arterial blood pressure was already elevated before the onset of choked disc, still high in the early stage, then decreased to normal in the efflorescent and below normal in the late stage. The same was found in the ratio of the retinal to the systemic blood pressure in each stage of chocked disc.

The retinal blood pressure was also elevated before the onset, moreover in the early stage, then decreased in the efflorescent stage to the level which was a little higher than the normal, and below the normal in the late stage.

It is practically important for the early diagnosis of choked disc that the retinal pressure was elevated not only in the early stage but also already before the onset.

The earlier the craniotomy was performed in patients with choked disc, the better the prognosis for the visual acuity. Therefore the ophthalmodynamometry is greatly valuable for the early diagnosis of brain tumor.

The differential diagnosis of papilledema in malignant hypertension from choked disc in brain tumor was performed very easily by ophthalmodynamometry, the retinal blood pressure being markedly higher in the former.

The ophthalmodynamometry is useless to determine the locality of the brain tumor. (3 tables, 22 references) (Published in Acta Ophth. Jap. 63:392, 1958 in Japanese.) Author's summary.

Van Balen, A. T. M. and Henkes, H. E. **Recording of the occipital lobe response in man after light stimulation.** Brit. J. Ophth. **44**:449-460, Aug., 1960.

The evoked occipital lobe response is triggered by an impulse starting in the retina. The amplitude is dependent upon the electrical properties of the subcortical center and the cortex. Probably the C^1 and C^2 waves represent the photopic and scotopic activity of the retina. Measurement may be made by electronic toposcopy or by mathematical averaging. (14 figures, 11 references)

Irwin E. Gaynon.

14

EYEBALL, ORBIT, SINUSES

Bottomley, S. S., Jarcho, L. W., Stowell, D. W. and Chatterley, J. G. **Unilateral exophthalmos.** A.M.A. Arch. Ophth. **64**:438-442, Sept., 1960.

A case of unilateral exophthalmos in a 27-year-old man is reported with demonstration of an intraorbital tumor by pneumotomography. This technique is presented as a safe and simple diagnostic method for such lesions. (3 figures, 11 references) Edward U. Murphy.

Frezzotti, R. **Transplantation of the temporal muscle into the orbital cavity after exenteration of the orbit.** Boll. d'ocul. **38**:801-812, Oct., 1959.

The author describes an exenteration of the orbit which was performed for malignant melanoma whose primary source was in the choroid. After the exenteration of the orbit a transplant of the temporal muscle was performed essentially by the introduction of the temporal muscle into the orbit through an opening in its lateral wall. In this case the author restored the conjunctival sac over the transplanted muscle on the twelfth day after the exenteration. A photograph of the final result shows a very excellent result. (10 figures, 1 reference) Joseph E. Alfano.

Paiva, C., Chaves, A and Gomes, A. **Postoperative micotic endophthalmitis.** Rev. brasil. oftal. **19**:193-202, Sept., 1960.

The authors described the case history of a patient who, after an uneventful intracapsular lens extraction, developed an area of deep corneal infiltration which progressed in spite of intensive local

treatment. A biopsy of this material was done and revealed the existence of a fungus, Hyalopus bogolepoffi. The corneal infiltration became worse, involving finally the entire eye. As there was no possible way of checking the spread of the disease, the eye was finally enucleated and the same fungus was found in every ocular tissue. (4 figures, 19 references)

Walter Mayer.

Winter, F. C. **Annual Reviews. The orbit.** A.M.A. Arch. Ophth. **64**:447-472, Sept., 1960.

This subject is reviewed from the literature of 1959 with some from 1958 and earlier. (140 references)

Edward U. Murphy.

15
EYELIDS, LACRIMAL APPARATUS

Eisner, Georg. **The usefulness of the Schirmer test.** Arch. f. Ophth. **162**:287-298, 1960.

The Schirmer test for the adequacy of lacrimation is found to be useful for clinical evaluation of lacrimal secretion but is not adequate for precise quantitative studies and statistical evaluation. (4 figures, 1 table, 33 references)

F. H. Haessler.

Hadija, K. G. **New method for the correction of entropion with trichiasis by tarsotomy.** Brit. J. Ophth. **44**:436-439, July, 1960.

In areas where the incidence of trachoma is high with much resultant scarring of conjunctivas and tarsal plates, a simple, tissue-saving procedure for correction of entropion is most beneficial. The author describes such a procedure which has been used in many cases with good results and a minimum of complications. After local anesthesia the lid is everted and the tarsal plate with its conjunctiva is lifted from the lid from below; it is elevated and reattached with a suture through the lid to a point several milimeters higher than originally. The effect of this is to evert the edge of the lid and so alleviate the trichiasis. This procedure has been satisfactorily used for three years. (4 figures) Morris Kaplan.

Harger, R. W. and Arata, L. A. **Vaccinia immune globulin used for vaccinia of eyelids.** J. Indiana M. A. **53**:1321-1323, 1960.

The authors describe vaccinia of the eyelids of the right eye in a child who had scratched a pustule on her arm which was the result of smallpox vaccination and transferred the lesion. Treatment with vaccinia immune globulin was entirely successful. An excellent color plate displays the appearance of six stages of the lesion. (2 figures, 6 references)

F. H. Haessler.

Massimeo, A. **A rare case of fibroma of the lower lids.** Boll. d'ocul. **38**:693-705, Sept., 1959.

The author presents a case of a 65-year-old woman with huge pendulous fibromas of the lower lids of 10 years' duration. The fibromas were excised and that of the right lower lid weighed 62 grams while that of the left lower lid weighed 240 grams. Histologic examination revealed diffuse fibrous formation with xanthomatous degeneration. (11 figures, 22 references) Joseph E. Alfano.

Radnot, N. **The restoration of lacrimal passages in cases without lacrimal sac.** Ophthalmologica **139**:450-453, June, 1960.

This report from the first university eye clinic in Budapest again brings out the fact that the dacryocystectomy (except in cases of tumors of the sac) has been completely replaced by external dacryocytorhinostomies for the success of which large, properly placed openings in the bone and carefully united mucous membrane flaps are essential.

In cases in which the sac has been com-

pletely or almost completely destroyed or obliterated the author has obtained good results with a modified dacryocystorhinostomy. The sac residue is split into a medial and lateral wall. The nasal mucosa is incised along the anterior and upper edge of the opening in the bone and joined, by means of sutures, to the small medial residue of sac mucosa. The lateral residue is sutured to a subcutaneous tissue flap obtained from in front of the opening in the bone. "By this method more than 20 cases have been operated on by us successfully during the last two years." (3 figures, 3 references)

Peter C. Kronfeld.

Valu, L. **Report on 455 lacrimal sac operations.** Ophthalmologica **139**:443-449, June, 1960.

Between 1951 and 1957, 455 lacrimal sac operations were performed at the university eye clinic in Debrecen (Hungary); 432 of these operations were dacryocystorhinostomies, nine were canaliculorhinostomies, four conjunctivorhinostomies and 10 conjunctivo-dacryorhinostomies after Stallard. About 94 percent of the dacryocystorhinostomies and between 30 and 50 percent of the other operations were successful. The series did not include a single dacryocystectomy. (1 table, 16 references) Peter C. Kronfeld.

Winkelman, J. E. **An operation for eversion of the lower lacrimal punctum.** Ophthalmologica **139**:486-487, June, 1960.

The author describes and advocates the transplantation of the lower punctum together with about 5 mm. of lower canaliculus into the lower fornix. (2 figures)

Peter C. Kronfeld.

16
TUMORS

Barishak, Y. R. **Differential diagnosis of melanoma cells in tissue cultures of uveal melanomas.** A.M.A. Arch. Ophth. **64**:367-376, Sept., 1960.

By the use of stains and histochemical reactions an attempt was made to distinguish melanoma cells from other cells in tissue cultures of uveal melanomas. A clear-cut differentiation could not be made. (16 figures, 27 references)

Edward U. Murphy.

Barishak, Y. R., Wanherick, W., and Yoneda, C. **Tissue culture of uveal malenomas.** A.M.A. Arch. Ophth. **64**:352-366, Sept., 1960.

The cells of 19 of 25 uveal malanomas were cultured successfully up to six months and studied carefully. Various theories as to the origin of melanoma cells and uveal pigmentation are reviewed but no definite conclusions could be reached from these experiments. (21 figures, 55 references) Edward U. Murphy.

François, J., Rabaey, M. and Lagasse, A. **Electron-microscopic data on pigment formation in melanoblastomata.** A.M.A. Arch. Ophth. **64**:377-381, Sept., 1960.

These studies suggest that pigment granules arise from a transmutation of mitochondria. (5 figures, 16 references)

Edward U. Murphy.

Vozza, R. **Bilateral symmetrical subconjunctival lipoma.** Boll. d'ocul. **38**:737-743, Oct., 1959.

The author presents a case of a bilateral symmetrical subconjunctival lipoma in a 78-year-old white male which was excised. A brief review of the literature is also presented. (2 figures, 28 references)

Joseph E. Alfano.

17
INJURIES

Barsky, David. **Eye injuries due to power lawn mowers.** A.M.A. Arch. Ophth. **64**:385-387, Sept., 1960.

Five cases of such injury are reported with total loss of vision in one patient and loss of the globe in two. The need for safety features in the rotary type is stressed. (4 figures, 3 references)

Edward U. Murphy.

Crawford, Bruce. **Peripatetic intraocular foreign body.** A.M.A. Arch. Ophth. **64**:392-395, Sept., 1960.

A non-magnetic foreign body just behind the lens in a seven-year-old boy was treated conservatively. It appeared in the anterior chamber 13 weeks after injury and was easily removed. (3 figures)

Edward U. Murphy.

Fiorini, G. **Cilia in the anterior chamber.** Boll. d'ocul. **38**:730-736, Sept., 1959.

The author presents a case of multiple cilia in the anterior chamber with secondary iridocyclitis and cataract formation. Three months later the cataract was of sufficient density to require removal; the cilia were adherent to its anterior capsule. (2 figures, 33 references)

Joseph E. Alfano.

18
SYSTEMIC DISEASE AND PARASITES

Chatterjee, B. M. and Sen, N. N. **Acute myeloid leukemia with leukemic deposit in the orbit.** Brit. J. Ophth. **44**:440-442, July, 1960.

In cases of lymphatic leukemia instances of orbital infiltration are frequently seen whereas in myeloid leukemia this occurs very rarely. Such a rare case was seen in a five-year-old Hindu boy who presented himself with a marked right exophthalmos. A hard mass could be felt above the lower orbital margin which obviously had forced the eye up and out. The vision and the fundus of the eye were unaffected. The child appeared otherwise normal but blood study revealed the presence of acute myeloid leukemia. The mass was easily removed and proved to be a focal collection of leukemic cells in a dense fibrous matrix. This tumor must be differentiated from chloroma which also occurs in this disease but which is a green pigmented mass. (2 figures, 17 references) Morris Kaplan.

Day, R. M. **Ocular manifestations of thyroid disease.** A.M.A. Arch. Ophth. **64**:324-341, Sept., 1960.

Evaluation of the ocular signs in 200 patients with thyroid dysfunction did not support the concept of Mulvaney and others that there are two distinct and mutually exclusive groups: the thyrotoxic and thyrotropic. The differences seem to be one of degree. At one extreme there is almost always upper lid retraction. At the other, the severe signs appear such as orbital infiltration, chemosis, and extraocular muscle involvement. An attempt to use goldfish in a controlled laboratory study of this problem was unsuccessful. (1 figure, 7 tables, 115 references)

Edward U. Murphy.

De Almeida, A. **Histopathology of diabetic ocular lesions.** Rev. brasil. oftal. **19**:187-191, Sept., 1960.

The author describes briefly the main pathologic findings in such diabetic changes as edema, pigmentary changes, glycogenic degeneration and rubeosis iridis, diabetic cataract and such retinal changes as lipoid changes of endothelial cells in the veins, microaneurysms, exudates, hemorrhages and retinitis proliferans. (1 figure, 6 references)

Walter Mayer.

Miettinen, P. and Wasz-Hoeckert, O. **Ophthalmological aspects of tuberculous meningitis.** Acta ophth. Suppl. 61, 1960.

The authors observed 193 children with tuberculous meningitis between 1949 and 1954 in the Children's Clinic of the University of Helsinki; 67 had concomitant

miliary tuberculosis, 17 patients were treated with streptomycin alone, 102 with streptomycin and PAS, 37 with streptomycin, PAS and isoniazid, and 37 with these drugs and cortisone. Eye complications were present in 125 cases (65 percent). For the patients with eye symptoms the mortality among the meningitis patients was 44 percent, among those with meningitis and miliary tuberculosis 66 percent. It was 21 percent for meningitis patients with no eye symptoms and 30 percent for the patients with miliary tuberculosis. The most common eye symptom were papilledema (41 percent), pupillary disturbances (21 percent) and choroidal tubercles (16 percent; other signs were muscle palsies and nystagmus. Pupillary disturbances and nystagmus were the most dangerous signs; mortality in these groups was 78 and 83 percent respectively. No differences were observed as to the palsies in the four treatment groups. The recovery time of patients with papilledema, however, fell from nearly three months to below one month.

Cicatrization of choroidal tubercles showed an even clearer difference. With streptomycin alone the recovery time was six months, with streptomycin and PAS under five months, with additional INH four months and with these drugs and cortisone less than two months. (54 tables, 27 references) John J. Stern.

Sheikh, M. E. **Vitamin deficiencies in relation to the eye.** Brit. J. Ophth. **44**:406-414, July, 1960.

Vitamins are essential elements for complete normal metabolism and when these are deficient, definite signs and symptoms of disease develop, especially so in childhood in periods of growth, during heavy work, in childbirth and lactation. Diagnosis of true vitamin deficiency is not always easy but one of the more practical methods of diagnosis is disappearance of the symptoms with administration of the vitamin. The deficiency is usually multiple but in ocular pathology the lack of vitamin A is the most important while the B complex is also frequently involved as a cause. In this series, 1,265 patients were examined for vitamin deficiency in the Nile River area and of these 85 percent were found to have typical signs and symptoms of multiple avitaminosis. The most common deficiency was that of vitamin A which was found in 56 percent; 24 percent of the patients had a deficiency of vitamin B, and 5 percent were deficient in vitamin C. Xerophthalmia was found in 409 subjects of which many had corneal xerosis with complete mummification of both corneas. It is suggested that general diseases such as anemia and schistosomiasis might well be associated as conditioning factors since they were found to co-exist in such a large number of the patients. It was further suggested that night blindness due to avitaminosis is most probably due to lack of both A and B rather than A alone. (5 figures, 13 references) Morris Kaplan.

19

CONGENITAL DEFORMITIES, HEREDITY

McMaster, P. R. B. **Decreased aqueous outflow in rabbits with hereditary buphthalmia.** A.M.A. Arch. Ophth. **64**:388-391, Sept., 1960.

Ten enucleated buphthalmic eyes were compared with 10 controls and decreased facility of outflow was recorded. (1 figure, 1 table, 10 references)

Edward U. Murphy.

Warburg, M. **Anophthalmos complicated by mental retardation and cleft palate.** Acta ophth. **38**:394-404, 1960.

The author provides a short historical review and describes one case. (4 figures, 1 table, 17 references) John J. Stern.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, *Cincinnati 19, Ohio*

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

ANNOUNCEMENTS

NEW YORK UNIVERSITY COURSES

New York University Post-Graduate Medical School, Department of Ophthalmology, New York, offers the following courses:

Ophthalmic plastic surgery, a part-time course, from 2:00 to 5:00 P.M. February 27th through March 3rd, under the direction of Dr. Sidney A. Fox. This covers the essentials of ophthalmic plastic surgery for the practicing ophthalmologist. Tuition: $90.00.

Motor anomalies of the eye, a full-time course given in two parts, under the direction of Dr. Harold W. Brown. Part I is for six days, March 6th through 11th. Tuition: $115.00. Part II is for five days, March 13th through 17th. Tuition: $100.00.

Surgery of the eye, a full-time course, March 20th through 25th, under the direction of Dr. Rudolf Aebli. This course includes lectures and practical work on the cadaver. Tuition: $140.00.

For further information write to: The Dean, New York University Medical School, 550 First Avenue, New York 16, New York.

KERATOPLASTY COURSE

A course on keratoplasty will be presented at the Presbyterian Medical Center of San Francisco on March 8th, 9th, and 10th, under the chairmanship of Max Fine, M.D. The enrollment is limited. Address inquiries to: Secretary, Eye-Bank, 2018 Webster Street, San Francisco 15, California.

INSTITUTE OF AMERICAS

The Institute of Ophthalmology of the Americas of the New York Eye and Ear Infirmary announces the following courses:

1. *Retinal detachment surgery.* Prof. Ernst Custodis, Director, Eye Clinic, Academy of Medicine, Düsseldorf, Germany. A series of three lectures to be given March 27th through 29th. Fee: $30.00.

2. *Pleoptics.* Dr. Heinz Gortz, Docent, Academy of Medicine, Düsseldorf, Germany. A series of two lectures to be given March 30th and 31st. Fee: $20.00.

Applications may be made to Mrs. Tamar Weber, Registrar, 218 Second Avenue, New York 3, New York.

OPHTHALMIC PLASTIC SURGERY

A three-week intensive course in ophthalmic plastic surgery will be conducted in New York, March 20th through April 7th. The course will consist of lectures, sessions in doctors' offices, preliminary and follow-up cases that are operated on during the time of the course, moving picture demonstrations of various ophthalmic plastic procedures, observation and assistance at the operating table on actual surgical cases, cadaver work and lectures and demonstrations and ancillary subjects such as photography, pathology, and X-ray radiation.

Anyone interested should contact the Registrar of the Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary or any of the following: Dr. Wendell L. Hughes, Hempstead, New York; Dr. Byron C. Smith, New York, or Dr. J. Gordon Cole, New York.

CONTACT LENS COURSE

The University of Texas Postgraduate School of Medicine announces the second annual contact lens course, scheduled for April 19th, 20th and 21st, in Houston, Texas. The reception of the first course was such that it was decided to repeat the course annually.

The instructors for this course are ophthalmologists skilled in this field, and experienced teachers. This course is designed so that those completing it will be proficient in all phases of contact lens fitting and adjusting. A departure in the teaching technique will be the use of closed circuit television during the didactic part of the course.

The course will be limited to 35 board-certified ophthalmologists or residents and fellows in ophthalmology. Registration for this course will close February 28, 1961.

For further information write: Office of the Dean, The University of Texas Postgraduate School of Medicine, 410 Jesse Jones Library Building, Texas Medical Center, Houston 25, Texas.

MICHIGAN CONFERENCE

The annual ophthalmology conference at The University of Michigan Medical Center will be held April 24th, 25th and 26th, under the direction of Dr. F. Bruce Fralick, chairman, Department of Ophthalmology. Applications may be addressed to the Department of Postgraduate Medicine, University Hospital, Ann Arbor, Michigan.

TRAVEL TO NEW DELHI

A large number of American ophthalmologists wish to attend the XIX International Congress of Ophthalmology to be held at New Delhi, India, on December 3-7, 1962.

Plans are under way to arrange for group transportation to New Delhi and for pre- and post-congress tours. The advantages and financial savings which will accrue because of group travel are considerable. In order to fit plans to meet the needs of the entire group, inquiries should be sent before March 1, 1961, to Peter H. Ballen, M.D., 131 Fulton Avenue, Hempstead, New York.

Spring postgraduate courses

The Institute of Ophthalmology of the Americas of the New York Eye and Ear Infirmary announces that the following postgraduate courses will be given this spring:

1. *Ocular surgery,* including lacrimal sac surgery, glaucoma, retinal detachment, cataracts, enucleation and evisceration, keratectomies and keratoplasties, anomalies of extraocular muscles, including ptosis, and orbitotomy, April 24th to 29th. Limited to 20. Fee: $225. Individual parts of the course may be taken at a prorated fee.

2. *Histopathology of the eye,* given under the direction of Drs. Bernard Roberts and Lawrence Samuels, May 1st through 6th. Limited to 15. Fee: $100.

3. *Practical aspects of perimetry,* given under the direction of Dr. Mortimer Cholst, May 3rd through 5th. Limited to 15. Fee: $40.

For registration, please apply to Mrs. Tamar Weber, Registrar, Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary, 218 Second Avenue, New York 3, New York.

Travel funds for junior investigators

Funds to cover the cost of round trip air coach travel are available to junior investigators engaged in or receiving training in the neurologic, otolaryngologic, and related sciences who plan to attend the following international meetings:

1. Seventh International Congress of Neurology, September 10-16, Rome, Italy.
2. Fifth International Congress of Electroencephalography and Clinical Neurophysiology, September 7-13, Rome, Italy.
3. Fourth International Congress of Neuropathology, September 4-7, Munich, Germany.
4. Seventh International Congress of Otorhinolaryngology, July 23-29, Paris, France.

Requests for these travel funds can be made by letter addressed to the Executive Secretary of the Selection Committee: Dr. Adolph L. Sahs, Department of Neurology, State University of Iowa, Iowa City, Iowa. The letter should include a brief summary of the applicant's educational, occupational, and research background, and should indicate his major field of interest. The letter should be signed by the applicant and countersigned by his administrative executive. The deadline for the receipt of requests is March 1, 1961. The Selection Committee will inform applicants of its action by April 15, 1961.

Funds for this purpose have been made available through grants to the Selection Committee from The National Institute of Neurological Diseases and Blindness, Public Health Service, and the National Science Foundation.

Ohio State postgraduate course

The Ophthalmology Postgraduate Conference of the Ohio State University School of Medicine, Columbus, Ohio, will convene on 8:00 A.M. on Monday March 6th and continue through March 7th. Speakers will be Dr. James M. Andrew, Dr. Jack Bontley, Mr. Joseph L. Bitonte, Dr. H. Richard Blackwell and Dr. William H. Havener of Columbus, Ohio; Dr. Bayard H. Colyear, Jr., San Francisco, and Dr. Joseph H. Haas, Chicago.

The program will include: "Management of suppression amblyopia," Dr. Havener; "Early diagnosis and management of retinal detachment," Dr. Colyear; "Chronic narrow-angle glaucoma," Dr. Haas; "Complications from the wearing of contact lenses," Dr. Makley; "The Institute for Research in Vision," Dr. Blackwell; "Surgical treatment of open-angle glaucoma," Dr. Haas; "Correction of anisometropia with special reference to contact lenses," Dr. Bontley; "Diagnosis of peripheral retinal disease," Dr. Colyear; "Physiologic variations in the tonographic tracing," Dr. Haas; "Fluorescein patterns in contact lens fitting," Mr. Bitonte; "The vitreous body," Dr. Colyear; "Complications of extraocular muscle surgery," Dr. Andrew.

The meetings will take place in the Ohio Union Building Conference Theatre. The registration fee is $20.00. For further information write to William H. Havener, M.D., Department of Ophthalmology, University Hospital, Columbus 10, Ohio.

New Orleans Academy

The midwinter convention of the New Orleans Academy, from February 19 through 24, will feature a "Symposium on strabismus." On the panel will be Dr. David G. Cogan, Boston; Dr. Goodwin Breinin, New York; Dr. Arthur Jampolsky, San Francisco; Dr. John Henderson, Ann Arbor; Dr. Edmond Cooper, Detroit; Dr. Marshall Parks, Washington, D.C.; and Dr. Harold Brown, New York.

The registration fee of $75.00 includes associate membership in the academy for the year 1961, as well as all other features of the convention. Hotel reservations should be made early by writing directly to the Executive Secretary, P.O. Box 469, New Orleans 1, Louisiana.

Washington Hospital Center

The Saturday morning lectures of the Department of Ophthalmology of the Washington Hospital Center for the month of March include:

March 4th, "Written examinations of probable Board questions and question and answer period," Drs. Bain, Caldemeyer and Seward. March 11th, "Contact lenses," Miss Pauline Long. March 18th, "Sensory physiology," Dr. Marshall M. Parks. March 25th, "Motor physiology," Dr. Francis Heed Adler.

Neurology congress

The VII International Congress of Neurology will be held in Rome, Italy, September 10th through 15th, under the auspices of the World Neurologic Federation and the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland. For further information write to Dr. Raffaello Vizioli, Viale University, Rome 30, Italy.

Vancouver meeting

Dr. Joaquin Barraquer of Barcelona, Spain, will be a guest speaker at the spring British Columbia Oto-Ophthalmological Conference to be held in Vancouver, B.C., on May 17th, 18th, 19th and 20th. He will give lectures and films on "Enzymatic zonulolysis," "Modern organization of surgical equipment," "Total reconstructive keratoplasty," "Acrylic keratoplasty," and "Acrylic lenses in anterior chamber."

Dr. Alfred Elliot, professor of ophthalmology, University of Toronto, will be giving several lectures and one or two papers by society members will complete the program.

Dr. Garnet Badger, Secretary, 925 West Georgia Street, Vancouver 1, B.C., will provide further information on the meeting.

Societies

Montreal meeting

At the recent meeting of the Montreal Ophthalmological Society at the Royal Victoria Hospital, the following program was presented: "Hemangioma of the choroid," Dr. Angus L. MacLean, Baltimore; "Morphologic and biochemical development of the lens," Dr. J. Langman, Montreal; Observations on the clinical determination of scleral rigidity," Dr. David A. Rosen, Kingston, Ontario, "Indications and contraindications for light coagulation," Dr. W. Hoepping, Essen, West Germany, "The A-V syndromes," Dr. Gordon M. Bruce, New York.

Southern Medical Association

At the meeting of the Southern Medical Association in Saint Louis, Missouri, the following officers were elected for the Section on Ophthalmology and Otolaryngology for the coming year: Chairman, Dr. Miles L. Lewis, Jr., 1539 Delachaise Street, New Orleans, Louisiana; chairman-elect, Dr. Samuel D. McPherson, Jr., 1110 West Main Street, Durham, North Carolina; vice chairman, Dr. Claude D. Winborn, 3707 Gaston Avenue, Dallas, Texas; secretary, Dr. Albert C. Esposito, First Huntington National Bank Building, Huntington, West Virginia.

The next meeting of the section will be held in Dallas, Texas, in November, 1961. Those interested in participating should write to the secretary of the Section, Dr. Albert C. Esposito.

International College of Surgeons

The Section on Ophthalmology of the International College of Surgeons held their meeting recently during the XII Biennial Congress at the Palazzo dei Congressi alle E.U.R., the site of the Olympics this past summer, in Rome Italy.

Prof. Giambattista Bietti, professor of clinical ophthalmology at the University of Rome School of Medicine, presided and the following ophthalmologists from the United States participated in presenting papers and being members of symposiums:

Dr. Paul A. Chandler of Boston, Massachusetts, was moderator of the panel on "Flat anterior chambers" and he spoke on "Flat anterior chambers after intraocular surgery." Dr. Albert C. Esposito of Huntington, West Virginia, spoke on "Cataract and allied ocular surgery." Dr. Robert J. Schillinger of Los Angeles, California, spoke on "Mechanical zonulysis in cataract surgery." Dr. Joseph E. Alfano of Chicago, Illinois, spoke on "Surgical management of orbital tumors." Surgical clinics were held at the University Hospital of the medical school.

West Virginia meeting

The West Virginia Academy of Ophthalmology and Otolaryngology will hold its annual meeting at the Greenbriar Hotel, White Sulphur Springs, West Virginia, on April 6th, 7th, and 8th. The guest speakers in ophthalmology will be Dr. Irving H. Leopold, Philadelphia, and Dr. Harvey E. Thorpe, Pittsburgh. In addition to the scientific program, arrangements have been made with Mr. Philip Salvatori of Obrig Laboratories to discuss and show techniques of contact lens fitting. For additional information please contact the secretary, Dr. Worthy W. McKinney, 109 East Main Street, Beckley, West Virginia.

The new officers of the West Virginia Academy of Ophthalmology and Otolaryngology are: President, J. A. B. Holt, Charleston; president elect, Albert C. Esposito, Huntington; vice president, William K. Marple, Huntington; secretary-treasurer, Worthy W. McKinney, Beckley, West Virginia; directors, James T. Spencer, Charleston, and Alan Fawcett, Wheeling.

Oklahoma City Academy

The annual spring meeting of Oklahoma City Academy of Ophthalmology and Otolaryngology with the Postgraduate Department of the University of Oklahoma Medical Center will be held on March 2nd and 3rd. Guest speakers will be: Ophthalmologists, Dr. James H. Allen, New Orleans, and Dr. Roscoe Kennedy, Cleveland. Otolaryngologists, Dr. Z. Z. Godlowski, Chicago, Dr. William House, Los Angeles, and Dr. Harold Tabb, New Orleans.

For further information, write to Dr. E. Norris Robertson, Jr., 301 N.W. 12th Street, Oklahoma City, Oklahoma.

Brooklyn meeting

The 158th regular meeting of the Brooklyn Ophthalmological Society was held on November 28th. The scientific program included "The Brooklyn-Queens glaucoma survey, May, 1960: Methods and

data," Dr. Bernard Schwartz; and "Follow-up of suspect glaucoma patients," Dr. Samuel Minowitz. A paper on "Acute angle-closure glaucoma," was presented by Drs. Joseph T. Menaker and Bernard Schwartz. "The diagnosis of glaucoma," was discussed by Dr. W. S. Knighton.

Officers of the society are: President, Dr. Ira W. Mensher; vice president, Dr. Edward Saskin; secretary-treasurer. Dr. Nicholas P. Tantillo; associate secretary-treasurer, Dr. A. Benedict Rizzuti.

Long Island society

Dr. Donald M. Shafer presented a paper at the November meeting of the Long Island ophthalmological Society. The subject of his address was "Retinal detachment."

New Mexico-Kansas Meeting

A combined meeting of the New Mexico Ophthalmological Society and the Kansas City Society of Ophthalmology and Otolaryngology will be held March 23rd, 24th, and 25th at Santa Fe, New Mexico. Guest speakers will be Dr. Harold G. Scheie and Dr. Albert N. Lemoine, Jr.

Personals

Dr. Dan M. Gordon of New York was guest speaker at the November 30th meeting of the Atlanta Eye, Ear, Nose and Throat Society. His subject was "Therapy in uveitis."

Dr. Walter H. Fink, clinical professor, Department of Ophthalmology, University of Minnesota, delivered the third University of Toronto Walter W. Wright Lecture in Ophthalmology at the Academy of Medicine on November 18th. He spoke on "Anatomic basis for vertical muscle surgery." The Walter W. Wright Lectureship in Ophthalmology was established two years ago in honor of Dr. Walter W. Wright, professor emeritus of ophthalmology, University of Toronto.

CONTENTS

(Continued from advertising page xxxv)

Correspondence

Treatment of herpetic keratitis by cauterization with silver nitrate 182
Correction: Chymotrypsin in dendritic ulcer 183
References omitted 183

Book Reviews

Anatomy: A Regional Study of Human Structure 184
Eye Signs in General Disease 184
Transactions of the Ophthalmological Society of the United Kingdom: Volume LXXIX ... 184
Industrial Arts for Blind Students 185

Abstracts

Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Tumors; Injuries; Systemic disease and parasites; Congenital deformities, heredity 186

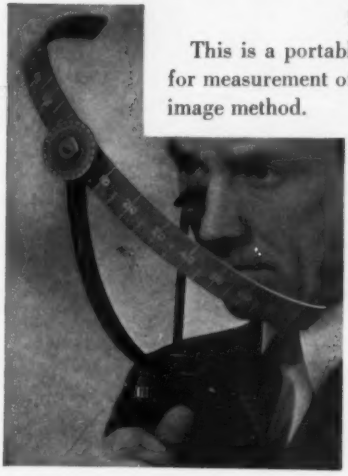
News Items 213

MATALENE

SURGICAL INSTRUMENTS CO., INC.

GRAND CENTRAL PALACE BUILDING—480 LEXINGTON AVE. at 46th STREET,
NEW YORK 17, N.Y.

SUCCESSORS TO THE E. B. MEYROWITZ SURGICAL INSTRUMENTS CO., INC.



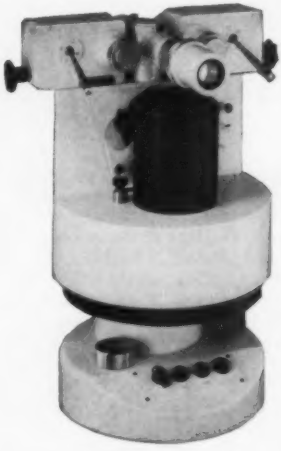
SCHWEIGGER HAND PERIMETER

This is a portable instrument adapted for plotting perimeric fields or for measurement of monocular rotation by the corneal reflex or Purkinje image method.

The instrument is held by the patient with a plate against the inferior margin of the orbit to fix the position of the arc before the eye. The arc has a radius of 17 cm and covers a field of 180 degrees. It may be rotated to any desired angle and a graduated disc indicates the angle in use. The arc is marked in degrees.

The perimeter folds flat so that it is easily portable but is sufficiently sturdy for routine examinations in the office. It is nicely finished in gray and is supplied complete with test objects, a wand and record charts.

Price $36.50



Pleoptophor
After Bangerter

A new instrument for the treatment of amblyopia, combining the best known up-to-date methods, like the dazzling-stimulating method of Bangerter and the after-image method according to Cueppers. This is an important step forward in the training of central fixation.

Ophthalmological Instruments of Top Quality

ALFRED P. POLL

40 WEST 55TH STREET, NEW YORK 19, N.Y.

Plastic tips are shielded allowing light to emerge only at the working point.

Tips available are:

"A" Globe retractor for Retinal-Detachment Surgery.
"B" Posterior Globe Illuminator.
"C" Anterior Illuminator.
"D" Focal Illuminator.
"E" Cobalt Blue for use with Fluorescein in Contact Lens fitting and Corneal examination.
"F" Multi-Spot, Six combinations of Red, Green and White for Color and Binocular Vision tests, Retinal Response in Cataract and Fixation.

Available in three sets:

Complete set of Light and six tips less batteries	$35.00
Retinal Detachment set, Light and tips "A,B,C,D"	$22.50
Diagnostic set, Light and tips "C,D,E,F"	$22.50
Long Life Mercury Batteries, each	$ 1.00
Tip Adapter for Welch Allyn Transilluminator	$ 2.75

Available at all Optical and Surgical Suppliers
Manufactured by

225 Cadwalader Avenue **R. O. GULDEN** Philadelphia 17, Penna.

Schiotz Tonometer Standardization—Repair—Maintenance service.

in contact lenses

Concentra® Corneal Lenses
Lacrilens® Molded Plastic Lenses
Solutionless Contact Lenses
Plastic Contact Trial Sets
Plastic Spherical Contact Lenses
Prism Contact Lenses
Cylindrical Contact Lenses
Plastic Microscopy Lenses
Plastic Gonioscopic Lenses
Colored Contact Lenses
Tinted Contact Lenses
Wetting Solutions
Plastic Molding Shells
Molding Equipment
Radius Gauges
Thickness Gauges
Textbooks

IT'S OBRIG FOR EVERYTHING IN SIGHT

A pioneer in plastic contact lens development and manufacture, Obrig Laboratories maintains leadership in the contact lens field through continuous, imaginative research. In experience, facilities and range of products and services, Obrig will not be surpassed. The list of Obrig products is a growing one; to its customers Obrig offers consultation and assistance in problem fitting cases. In contact lenses – it's Obrig for everything in sight.

Obrig Laboratories, Inc.

75 East 55th Street, New York 22, N.Y. · PLaza 8-0960
Florida: P. O. Box 791, Sarasota
Foreign Branches: Montreal, Canada / Johannesburg, South Africa / San Jose, Costa Rica / Caracas, Venezuela

BAILLART OPHTHALMODYNAMOMETER

For measuring the pressure in the central artery of the retina. Especially valuable in early diagnosis of carotid artery occlusion.

This instrument is a simple spring-loaded pressure gauge. As it is pressed against the sclera, increasing intraocular tension causes the retinal arteries to pulsate. When pulsation begins, the thumb screw is set and a reading taken for diastolic pressure. More pressure is then applied until pulsation ceases, when systolic pressure is determined. The test requires no special skill in ophthalmology.

#40-5495 ..... $30.00

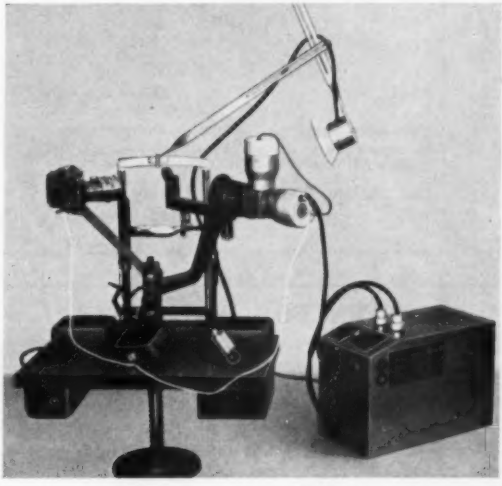
Prices F.O.B. factory Philadelphia. Subject to change without notice.

Order direct from

GEORGE P. *PILLING* & SON CO.

3451 Walnut Street • Philadelphia

Pilling New York Office—4 W. 56th St., New York 19, N.Y.
Other Offices: Columbus, Ohio—Atlanta, Georgia—Los Angeles, Calif.
CABLE ADDRESS: Surgical-Phila.



"OCULTRON"

ELECTRONIC FLASH PHOTO EQUIPMENT

FOR GOLDMANN (HAAG-STREIT) SLIT LAMP

Proper illumination for photography of all details normally visible with the slit lamp.

Developed at University Eye Clinic in Vienna, Austria.

Can be mounted easily by ophthalmologist himself.

Distributed in USA & Canada by:

ALFRED P. POLL

Ophthalmological Instruments of Top Quality

40 West 55th St., New York 19, N.Y.

WE Inc. *the contact lens specialty company*

CHICAGO
2345 WEST WOLFRAM STREET
LOS ANGELES
2023 WESTWOOD BLVD.
NEW ORLEANS
207 SOUTH SARATOGA STREET

SOLUTIONS
KITS and CASES
DIAGNOSTIC AIDS
OFFICE EQUIPMENT and SUPPLIES
LABORATORY EQUIPMENT and SUPPLIES

WAGTOWNE ENTERPRISE, Inc.

GREINER & MUELLER
Expert makers
of artificial human eyes
GLASS & PLASTIC
55 E. Washington St. . . . Chicago 2, Ill.
Phone FR 2-4449
Branches at Kansas City, Mo., Detroit, Mich.
Our experts visit Milwaukee, Madison, Minneapolis, and St. Louis regularly. Serving the Middle West since 1924.
Eye making has been a family tradition with us since 1835.

AN EMPLOYMENT REGISTRY FOR SCIENTISTS

in the basic sciences appertaining to OPHTHALMOLOGY AND OTOLARYNGOLOGY has been established by the American Academy of Ophthalmology and Otolaryngology. The Registry will aid in the placement of candidates completing training who desire academic and investigative positions, and in the replacement of those already in such positions who desire a different position. It will also serve institutions seeking to fill such positions.

Since the Registry will be of considerable service to scientists in the fields of Ophthalmology and Otolaryngology, it will be operated by the Academy without fee or obligation.

For further information and registry forms, write to

American Academy of Ophthalmology and Otolaryngology Registry
W. L. Benedict, M.D., Executive Secretary
15 Second Street S.W., Rochester, Minn.

The RHEO-TRAN Unit

- Provides greater illumination
- Fits large diagnostic handle
- Eliminates use of batteries
- No increase in weight

For Office, Hospital, Bedside

110 volts, A.C. only

RHEO-TRAN Unit only—$37.00, including one 3.8 bulb write for literature

Austin Belgard

OPHTHALMIC OPTICIANS

109 N. Wabash, at Washington
Chicago, Illinois

Why Substitute When You Can Have...

One of America's Finest Absorptive Lenses. Prescribe Genuine

Therminon LENSES

Thru All Reliable Laboratories
THERMINON LENS CORP.
63RD AT UNIVERSITY
DES MOINES, IOWA

THE UNIVERSITY OF MICHIGAN MEDICAL CENTER

Postgraduate Conference in Ophthalmology

The annual Conference in Ophthalmology will be held April 24, 25 and 26, 1961 at The Rackham Graduate School Building, Ann Arbor, Michigan.

Dr. F. Bruce Fralick and Staff of the Department of Ophthalmology will conduct the conference. The following named guest lecturers will participate:

Dr. Robert W. Hollenhorst, Rochester, Minnesota

Dr. Charles E. Iliff, Baltimore, Maryland

Dr. S. D. McPherson, Jr., Durham, North Carolina

Dr. Warren A. Wilson, Los Angeles, California

Applications may be addressed to the Department of Postgraduate Medicine, University Hospital, Ann Arbor, Michigan.

CHICAGO OPHTHALMOLOGICAL SOCIETY
1961 CLINICAL CONFERENCE

May 19 and 20, 1961 — **The Drake Hotel, Chicago, Illinois**

PRELIMINARY PROGRAM

GUEST SPEAKERS:

Count H. Arruga, M.D., Barcelona, Spain
Bernard Becker, M.D., St. Louis, Mo.
G. Leigh, M.D., London, England
Harold G. Scheie, M.D., Philadelphia, Pa.
Robert N. Shaffer, M.D., San Francisco, Calif.

SUBJECTS:

Retinal Detachment
Corneal Surgery
Symposium: "Surgery and Medical Therapy of Narrow and Open Angle Glaucoma"
Symposium: "Secondary Glaucoma"
Other subjects to be announced

Fee: $45.00 (Includes Round Table Luncheons and Dinner following Gifford Lecture)
Registrar: Mrs. Mary E. Ryan, 1150 North Lorel Avenue, Chicago 51, Illinois

---

THE SEVENTEENTH ANNUAL GIFFORD MEMORIAL LECTURE

Dr. Harold G. Scheie, Philadelphia, Pennsylvania
Friday, May 19, 1961, The Drake Hotel
5:15 P.M.

The Chicago Ophthalmological Society extends an invitation to all physicians to attend the Lecture. A dinner which follows is open to physicians and their wives.

URGENT REQUEST

The Uveitis Laboratory, University of California School of Medicine, San Francisco, is vitally interested in obtaining freshly enucleated eyes from patients with all types of uveitis and other endogenous inflammations. Attempts are being made to isolate etiologic agents from these eyes.

The eyes should be placed in a sterile bottle, packaged with the history and findings, and shipped as quickly as possible. Please send specimens special delivery, collect, and mark the package "Fresh Tissue Specimen—Rush." Do not freeze or use preservatives of any kind.

A report of isolations of organisms and pathologic findings, including a slide, will be sent to the contributor. Credit will be given in any resulting publications if desired.

Telegraph collect if specimen being sent.

Send eyes to
Samuel J. Kimura, M.D., Michael J. Hogan, M.D., or
Phillips Thygeson, M.D.
University of California School of Medicine
San Francisco 22

It Will Pay You

to look through the advertising pages of this Journal.

We discriminate as to the quality and reliability of the advertising accepted for the

AMERICAN JOURNAL
of
OPHTHALMOLOGY

PRESCRIPTION OPTICIANS

ST. LOUIS, MO.

Erker Bros. Optical Co.

908 Olive Street
518 N. Grand Boulevard
and 33 N. Central Ave., Clayton, Mo.
Prescription Opticians Since 1879

PORTLAND, ORE.

Hal. H. Moor, 315 Mayer Bldg.

Guild Optician

Oculists' prescriptions exclusively

For the Discriminating Eye Physician

Depend on the Services of a Guild Optician

IN LYNCHBURG, VA.

A. G. JEFFERSON

Ground Floor Allied Arts Bldg.

Exclusively Optical

L. M. Prince OPTICIANS

Specialists in filling ophthalmologists' prescriptions with utmost care.

Cincinnati, Ohio	4 West 4th St. 23 Garfield Pl. 411 Oak St.
Dayton, Ohio	117 S. Ludlow
Covington, Ky.	8th & Scott
Newport, Ky.	317 Monmouth

PERFECTION, SKILL, and SERVICE SINCE 1872

"OPHTHALMIC LITERATURE"

AN ABSTRACT JOURNAL IN ENGLISH OF THE WORLD'S CURRENT LITERATURE ON OPHTHALMIC SUBJECTS

Indispensable to the busy practitioner for quick reference and timely useful information.

"Ophthalmic Literature" and Index (8 numbers) Yearly subscription—Four Guineas ($13.50 U.S.A.). Published by British Medical Association.

U.S.A. Agent

MEDICAL MARKET RESEARCH, INC.
East Washington Square,
Philadelphia 5, U.S.A.

now...you can
really and properly
correct **astigmatism** with the
new, revolutionary Wesley/Jessen

CYCON* CONTACT LENS

(Fitting of an astigmatic cornea with a toric base curve contact lens)

Lacrimal distribution with spherical base curve

Lacrimal distribution with CYCON base curve

The CYCON Contact Lens successfully minimizes these problems:

corneal staining: The CYCON Contact Lens prevents rocking action across the astigmatism, thereby minimizing possible corneal staining.

rotation: The CYCON Contact Lens minimizes rotation. Less rotation means less movement, which usually results in less irritation.

unequal pre-corneal fluid layer: The CYCON Contact Lens creates a more equal lacrimal layer which allows for excellent lid pressure distribution across the cornea.

flare: With the CYCON Contact Lens, the patient is not looking through the peripheral section or edge of the contact lens. This lens tends to prevent the prismatic lacrimal layer, thus minimizing flare.

movement of lens: The CYCON Contact Lens tends to stabilize in position.

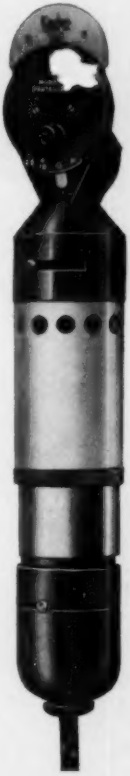
lid irritation: With a CYCON Contact Lens, there is less possibility of lid irritation, as the contact lens will fit closer to the cornea.

The ultimate in contact lens fitting is gradually being approached with the fitting of Wesley-Jessen CYCON Contact Lenses. The principles learned from Photo-Electronic-Keratoscopy (PEK*) will aid in the fitting of CYCON Contact Lenses. Please feel free to communicate with us for consultation on your problem cases of Astigmatism.

THE PLASTIC CONTACT LENS COMPANY
5 South Wabash Avenue
Chicago 3, Illinois

*Trademark

for the finest Ophthalmoscopes



KEELER Ophthalmoscopes mean perfection in performance, reliability and design.

The "SPECIALIST" has become the accepted battery-operated ophthalmoscope among the world's leading ophthalmologists. Its narrow beam, critically sized and angled, reduces corneal reflex to a minimum well outside the line of sight, thus permitting optimum view of macula. Alternative apertures provide three areas of illumination in the ratio 1:4:25.

The Modified PANTOSCOPE, designed specifically at the request of many users of the regular Pantoscope, gives the latter instrument's same superb vision but provides for direct and indirect ophthalmoscopy only. For a very powerful yet simple 'scope the MODIFIED PANTOSCOPE is the ideal choice.

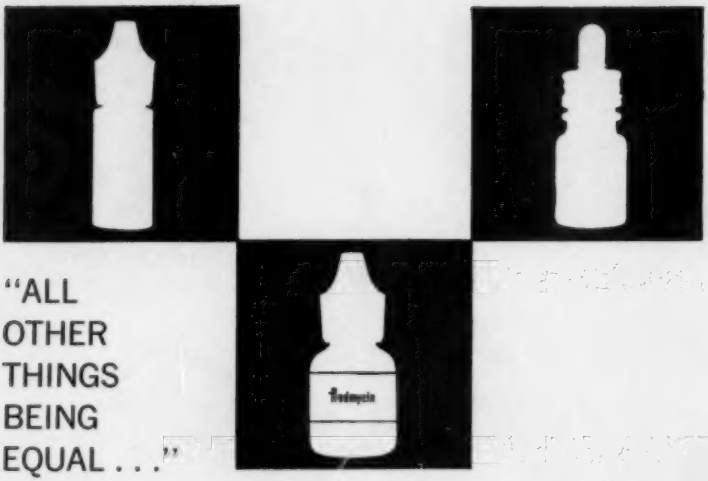
For every type of Ophthalmoscope . . . the automatic choice is a KEELER . . .

LITERATURE AVAILABLE FROM

KEELER OPTICAL PRODUCTS, INC.

5536 Baltimore Avenue Philadelphia 43, Pa.

Tels: GRanite 4-5310 & Kingswood 4-0874



"ALL
OTHER
THINGS
BEING
EQUAL . . ."

The familiar phrase above is often heard when a difficult choice is being made — it is usually concluded much this way . . . "let's take this one, it has that one feature I particularly like".

So it is with **Predmycin®**

In the treatment of ocular infection, PREDMYCIN Ophthalmic Solution offers neomycin (0.5%) and prednisolone (0.2%) for prompt control of infection and inflammation. But PREDMYCIN provides one important feature more—the decongestant, phenylephrine (0.12%) for rapid paling of the patient's eye. Actually, PREDMYCIN'S decongestant not only improves the look and "feel" of the eye, but also helps allay irritation, check further edema and localize the steroid in the tissues.

Pharmaceutically, PREDMYCIN is presented in a sterile, lubricating solution for rapid absorption . . . rapid therapeutic effect—available in 5 cc. plastic dropper bottles for maximum patient acceptance and convenience.

In short . . . for prompt, comprehensive relief of ocular infection PREDMYCIN *is a drug of choice.*

ALLERGAN PHARMACEUTICALS INC. Los Angeles 17, California